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BUREAU OF HYGIENE AND TROPICAL DISEASES.

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THE TOXICITY OF MEPACRINE IN MAN.

By G. M. FINDLAY, C.B.E., M.D., D.Sc., M.R.C.P.

General.

The pharmacology and therapeutics of mepacrine are now largely of historical interest; but its toxic effects still require some attention, since they may involve claims for compensation or pension. Single doses of 1·0 to 1·5 gm. have often been given without untoward effect, while larger doses of mepacrine have occasionally been taken either in error or with suicidal intent (BARBOSA 1934, FOY *et al.* 1936). BURNHAM (1946) recorded a case where a man took 90 grains (6·0 gm.) in an attempt at suicide: recovery was complete and no apparent signs of liver damage remained. MARKSON and DAWSON (1945), also, reported the case of a patient who, after taking 0·7 gm. of mepacrine weekly for 16 months as a suppressive, swallowed 250 tablets (25 gm.) with suicidal intention. Ten minutes later, he began to vomit and suffered from diarrhoea; he then became weak and drowsy. When he was found three hours later he was collapsed and stuporose; the skin was cold and clammy, the pulse barely perceptible, the pupils contracted and all tendon reflexes were highly active. The plasma mepacrine concentration was 906 μgm. per litre. On the second day the plasma mepacrine was 183 μgm. per litre, and on the third day it had fallen to 90 μgm. per litre. At no time was mepacrine found in the cerebrospinal fluid. The urine contained no albumin, bile, sugar or acetone. The patient was given adrenaline, 2 pints of 30 per cent. of glucose saline, and 5 mgm. of riboflavin intravenously; in twenty-four hours he had recovered. WRIGHT and LILLIE (1943), however, found that in rats given 80 mgm. mepacrine per kgm. of body weight the toxic effects were not reduced by a daily dosage of riboflavin, 5 to 10 mgm. per kgm. of body weight.

Occasionally, in patients who are given therapeutic doses of mepacrine, there are symptoms of nausea associated with abdominal discomfort (GREEN 1932, CHOPRA *et al.* 1933, SCHULEMANN 1935, HOOPS 1935). Among 49,681 cases which were treated with either prophylactic or therapeutic doses of mepacrine, however, BISPHAM (1941) found only 38 in which there were severe symptoms, vomiting, diarrhoea, anorexia, epigastric or precordial pain and restlessness.

During the war of 1939 to 1945, when mepacrine was taken as a suppressive by large numbers of troops, mild symptoms referable to the abdomen were common during the first ten to fifteen days of suppressive therapy, when nausea,

eructations, diarrhoea, and a feeling of fullness in the abdomen were experienced. These symptoms usually disappeared completely, but in about 2 per cent. of cases they continued and necessitated the withdrawal of mepacrine. Headache, insomnia, temporary giddiness and faintness were less common. Slight mental depression has been noted, but this is less than that associated with the prolonged taking of suppressive quinine (FINDLAY and STEVENSON 1944). During the war years, a number of surveys were made of the effects of mepacrine on volunteers in a cool climate, on troops who had returned to a cool climate after taking mepacrine for 12–18 months, and on troops still serving in the tropics who had taken 0·1 gm. mepacrine daily for periods of 1 to 3 years. No evidence could be found of damage to the respiratory, cardiovascular, haematopoietic or nervous systems, or to the functional activity of the liver or kidneys. Any abnormalities observed in the electrocardiogram could be attributed to other causes (LEVINE and ERLANGER 1946).

Severe Toxic Reactions.

Severe toxic reactions to mepacrine involve the skin, the central nervous system, haematopoietic system and the eyes.

(i) *Skin lesions.*

Even before the second world war, there had been occasional reports of skin lesions attributable to mepacrine. NAYADU (1937), for instance, described two patients with giant urticaria which was believed to be due to mepacrine, and STOREY (1938) observed a patient with round or oval macules on a diffuse erythematous background, a rash closely resembling that of endemic typhus: two days after the drug was discontinued the rash faded. In doctors and nurses handling mepacrine, skin lesions had also been seen; while in those exposed to an atmosphere containing mepacrine dust, lachrymation, photophobia and eczematous patches occasionally developed. WHITEHILL (1945) described the case of a nurse who, as a result of handling mepacrine, developed a contact dermatitis on both eyelids and behind the right ear. The yellow pigmentation of the skin was also well known (SONI 1935, SCHECHTER and TAYLOR 1936). Its intensity varies greatly in different persons. It is most clearly seen on the dorsal surfaces of the fingers and on the forehead and face but only very rarely on the sclerae. When the conjunctivae are tinted, the yellow colour is seen most distinctly on the parts not exposed to light. The yellow tint may last for two to four months after the taking of mepacrine is discontinued. It appears to be due to the staining of the tissues by an acridine dye which renders the tissues fluorescent. GINSBERG and SHALLENBERGER (1946) find that fluorescence on exposure to Wood's light disappears from the finger nails in from 3 to 6 months, while in the toe nails fluorescence may be detectable up to twelve months after administration of mepacrine. Apart from the aesthetic discomfort, which is specially felt by women, the yellow discolouration is of no consequence. A far less striking finding is a bluish-grey or slate-coloured pigmentation of the nail beds, either a diffuse pigmentation involving the entire nail bed, or a transverse band near the middle of the nail. Such bluish pigmentation may also involve the skin of the nose, the hard palate, the epiglottis and the tracheal rings and the skin of the sides of the nails. On the hard palate it is usually first seen near the midline when it spreads to the gum margins. It may vary in colour from slate-grey to blue-black. Biopsy specimens show that the pigment contains iron. It was by no means uncommon in Europeans in West Africa in those who had taken mepacrine for more than a year while it was also noted in the Pacific Area (LIPPARD and KAUER 1945, LUTTERLOH and SHALLENBERGER 1946). In American troops, this type of pigmentation was present in 27·3 per cent. of those

taking mepacrine for 7 to 12 months, in 54·8 per cent. of those taking mepacrine for 13 to 18 months, and in 63·8 per cent. of those taking mepacrine for 19 to 24 months. The blue pigmentary changes also fade in from two to three months.

Lichenoid dermatitis.—During the latter part of 1943, reports began to appear of a curious lichenoid skin disease which was becoming not uncommon among Australian and American troops fighting in the Pacific area. At first, as in the report by AMBLER (1944), the large number of patients suffering from lichen planus hypertrophicus was noted. Later the suspicion arose that these cases were in some way associated with the prolonged administration of mepacrine (HARVEY *et al.* 1944, SCHMITT *et al.* 1945, MITCHELL 1945, and others). For security reasons, much information was suppressed during the actual continuance of hostilities, but with the coming of peace it is now possible to give a full account of the subject.

The "mepacrine dermatitis complex," as it has been called, was seen in all theatres of war where, owing to the presence of malaria, suppressive mepacrine was necessary. It was most prevalent in the Pacific zone, though cases were reported from Australia, Burma, India (LIVINGOOD and DIEUAIDE 1945), Assam, North Africa and Italy (NELSON 1945, PETERKIN and HAIR 1946, and PETERKIN 1947), and West Africa. Its incidence, however, varied greatly in different areas. Even in the Pacific and South East Asia, the incidence was higher in some localities than in others, suggesting that climatic and geographic factors may have played a contributory rôle. No race appears to have been exempt, since cases were seen in Americans, British, Australians, Mexicans, Negroes, Filipinos, American Indians, Chinese and Japanese. Judging from the clinical reports which have appeared the disease seems to have been far more common among Americans than among other nationals, more than 1,000 cases having been reported by American observers (BUTLER (1947), 247 cases; BAZEMORE *et al.* (1946), over 400 cases; BERESTON (1946), 200 cases; EPSTEIN (1945), 65 cases; BAGBY (1945), 25 cases; DANTZIG and MARSHALL (1946), 24 cases; KIERLAND (1946), 49 cases; ROSENTHAL (1946), 5 cases). PETERKIN (1947) mentions only 53 British cases seen by him in the Mediterranean zone. In West Africa, the incidence of lichen planus and lichenoid conditions was no higher among British troops after March 1943, when mepacrine suppression was begun, than it had been in 1941 and 1942, when British troops were taking quinine; in addition, the incidence of lichen planus, and, incidentally, exfoliative dermatitis, was no higher among British troops in West Africa who were taking mepacrine than among African troops who were not taking any suppressive (FINDLAY 1946); only three cases of exfoliative dermatitis occurred in two years among 15,000 British troops. There is a suggestion from American sources that women, in proportion to their numbers, were more frequently affected than men in the South-West Pacific area, while brunettes were more often affected than blondes. Of 259 patients, 82 per cent. were brunettes (BAZEMORE *et al.* 1946). Temperamental differences were not significantly associated with the diseases. The condition, which at first was termed "atypical lichen planus," is characterized by various combinations of the following lesions: violaceous and erythematous, hypertrophic, lichenoid papules and plaques, often with a rough verrucous surface; violaceous and erythematous, oozing or scaling eczematoid plaques, well demarcated in some cases, ill-defined in others: flat, squamous, geographic, plaques on the trunk, axillae and groins, similar to tinea lesions; white, sometimes violet-tinged, slightly raised mucous membrane lesions identical with those seen in typical lichen planus; oozing intertriginous dermatitis in the groins, axillae and posterior surface of the ears; ecthymatous lesions; scaling and superficial fissuring of the lips and scaling erythematous eczematoid dermatitis of the

eyelids. In some patients the lesions are predominantly lichenoid, in others most of the plaques are eczematoid. Many patients have at some time both violaceous hypertrophic lichenoid plaques and some form of cutaneous eczematoid reaction. During the course of the disease, a considerable number of these patients suffer from acute "explosive" generalized exacerbations, manifested by oozing eczematoid dermatitis especially on the flexor surfaces of the limbs, the groins, axillae, extremities and neck. Such exacerbations merge into a true secondary exfoliative dermatitis, quite as severe as that seen in primary exfoliative dermatitis.

At the onset, the first appearance is usually that of localized violaceous or erythematous eczematoid plaques on the dorsal surface of the hands or feet, the upper part of the back, or on the sides of the neck, ears, nose and around the mouth. The plaques often appear first as tiny follicular papules 1 to 2 mm. in diameter, later coalescing to form the violaceous plaques 2 to 5 mm. in diameter. These plaques in turn fuse to form thick plates of violet-gray desquamating skin up to 30 cm. in diameter and sometimes as much as 1 cm. in thickness. The tops of the lesions are flat, and Wickham's striae are frequently seen; later the tops are covered with fine adherent silvery scales (BAZEMORE *et al.* 1946). The soles and palms are often solid plaques, which crack and bleed on motion. BARKER (1947) has noted hyperkeratosis of the palms and soles as the only symptom. The lesions were symmetrical and disappeared slowly as the yellow colour of the skin decreased. BAGBY (1945) has described five cases in which pustules were replaced in healing by lesions of atypical lichen planus. The polygonal shiny lesions characteristic of true lichen planus did not occur. After the appearance of the initial lesions, there was usually a generalization over the whole body, though not infrequently the middle zone of the trunk was exempt. The parts most severely affected were the legs, forearms, dorsal surfaces of the hands and feet, face and eyelids, buttocks, the sternum and neck and the genitalia. Lesions were particularly liable to develop at the sites of trauma and on areas recently affected by tinea or scabies. The site of the initial lesions in 302 patients is shown in Table I. In addition to the lichenoid plaques, some patients more rarely showed lesions resembling psoriasis or even pityriasis rosacea. Lesions of the mucous membranes also appeared, with blisters and ulcers in the mouth, fissures on the lips and at the corners of the mouth, and rawness on the edges of the tongue. The mucosa of the vagina or rectum was rarely involved, but BUTLER (1947) has described lesions resembling condylomata on the genitalia and in the perianal region.

The histological changes present in the skin have been very fully investigated by ROSENTHAL (1946). Three stages, which merge into each other, may be distinguished. The main features are the hyperkeratinization and plugging of the openings of the hair follicles, the degenerative and liquefactive changes in the basal layer, and the presence of infiltrating cells in the papillary and subpapillary connective tissue around the hair shafts, hair follicles and some of the dermal glands. The number of the invading cells, histiocytes, lymphocytes and eosinophiles, with very few polymorphonuclear leucocytes and plasma cells, depends on the severity of the disease. The changes in the basal layer are somewhat patchy and vary in different regions. They are best seen in the acute stage, but even then they may not be distinguishable from those of other dermatoses. There is no vascular or collagenous change other than that accompanying acute inflammation. Oedema is frequently seen in the acute and subacute stages, both extracellularly and intracellularly in the prickle cell and basal layers, as well as in the upper layers of the corium. Atrophy of sebaceous glands and infiltration around sweat glands are frequent. Of all the changes noted, the one that is common to all stages is the lesion in the

TABLE I.

The site of the Initial Lesion in Lichenoid Dermatitis.
(BAZEMORE *et al.* 1946.)

Location	No. of cases	Percentage of cases
Hands and wrists	103	33·7
Feet and ankles	72	23·8
Legs	49	16·2
Groin	12	4·0
Arms	11	3·6
Thighs	9	3·0
Eyelids	8	2·3
Ears	5	1·6
Lips	5	1·6
Face and scalp	5	1·6
Chest	4	1·3
Axillae	4	1·3
Mouth	3	1·0
Abdomen	3	1·0
Neck	3	1·0
Scrotum	3	1·0
Other sites	3	1·0

basal layer: this layer of the epidermis is the last to return to normal when the disease has subsided. An outstanding feature is the aggregation of pigment in the papillary and subpapillary connective tissue. These collections of pigment are specially seen in the acute stages, most characteristically at the tip of the papillae, but frequently also in the subpapillary connective tissue; the pigment is found either within macrophages or scattered in the connective tissue. It gives negative reactions for haemosiderin or haemofuscin but positive tests for melanin. The pigmentation is not limited to the acute stage but is found in appreciable amounts even in the papillary or subpapillary connective tissue. The normal pigment of the basal layer is generally increased.

Other forms of dermatitis.—In addition to the lichenoid lesions, a condition of eczematoid dermatitis has been seen in persons taking suppressive mepacrine. Bilateral symmetrical, violet-tinged, vesicular, eczematoid or oozing plaques occur and these involve more especially the hands, arms, feet, legs and less commonly other parts of the body. The nail-bed and skin of the nail-folds are frequently affected, resulting in exfoliation of the nails without true suppurative paronychia. The term 'symmetrical eczematoid dermatitis' has been applied to this condition (*Medical Consultants Division Rept.*, U.S.A. 1945). The lichenoid and the eczematous conditions may frequently be combined in the same patient. While a broad division may be made into those lesions that are raised above the skin surface and those that are not, it is possible to distinguish the following types, which together make up the mepacrine-dermatitis complex:—

(1) A non-weeping form, with the primary characteristics of a lichenoid dermatitis.
(2) Eczematous dermatitis.
(3) Combined lichenoid and eczematous dermatitis.
(4) Pustules replaced in healing by lichenoid lesions.
(5) Exfoliative dermatitis secondary to (1) to (4).
(6) Primary exfoliative dermatitis.
(7) Hyperkeratosis of the palms of the hands and soles of the feet.

A number of secondary complications have been described. There is usually loss of body-hair, while the scalp hair shows a condition recalling alopecia areata. When the hair returns, it is often darker than it was before. BAZEMORE *et al.* (1946) describe one case where the hair was at first white but later returned to normal. Total alopecia has occurred. When no hair is lost, groups of follicular papules may be seen on the hair scalp. Itching is sometimes severe and is not necessarily related to the severity of the lesions. In some instances, a prodromal stage was noted in which intense itching was present in the absence of lesions, Pruritus, also, did not correspond with the severity of the condition. Nervous phenomena occasionally occurred ; sharp shooting pains were present in the legs, patches of anaesthesia and paraesthesia in the skin and, in rare instances, disturbance of vision with contraction of the visual fields. Polyneuritis has also been seen. Mental depression was not infrequent, while BUTLER (1947) among 247 cases describes three in which there were hallucinations and delusions. Secondary bacterial infection with pustules or abscesses, sometimes with the formation of septic ulcers, was seen in about 10 per cent. of cases, and the lymph nodes, more especially those in the inguinal region often exhibited a non-suppurative adenitis : lymphangitis has occurred. Staphylococci and streptococci, diphtheroids and coliform organisms have been isolated. Infection of hair follicles, both superficial and furuncular, was common, the usual organism being *Staphylococcus aureus.*

Interference with sweating in the affected areas was very common. Some patients were sensitive to light. Venous stasis, with oedema in the lower limbs, was occasionally seen. Anorexia and diarrhoea were sometimes present ; in one patient, blood was passed *per rectum.* Most patients lost weight, decreases of 10 to 30 lb. (4·5 to 13·5 kgm.) being not infrequent. A low-grade fever was often present. Depigmentation or hyperpigmentation, with deposits of melanin and atrophy of the skin, were also encountered. In a negro, patches of vitiligo developed. Diffuse follicular accentuation in the skin over the upper part of the back, shoulders and extremities, and loss of, or changes in, the nails, were sometimes seen. Telangiectasia also occasionally developed. Simple anaemia was not uncommon and in a few patients aplastic anaemia occurred ; BERESTON and SASLAW (1946) described one patient who, in the course of an exfoliative dermatitis, showed symptoms of glomerulo-nephritis with albumin, red blood corpuscles and granular and pus casts in the urine. The skin became a dark coffee-colour and a profound anaemia developed (haemoglobin percentage 58, erythrocytes 2,810,000 per cmm.). A high eosinophil count, up to 54 per cent., was sometimes encountered in the absence of helminthic infection or Löffler's syndrome. As a rule liver function tests revealed no abnormality. A number of other complications have also been seen in association with the mepacrine dermatitis complex, but it is doubtful whether there was any causal relationship. Pericarditis, hepatitis, atypical pneumonia, ascites and oedema have all been recorded. In some cases, death has occurred. BUTLER (1947) records a fatal case in which death took place three months after the last dose of mepacrine. In this instance, degenerative changes were found in the myocardium.

During convalescence, recurrent attacks of pyoderma superimposed on the flattening lichenoid lesions may develop, while thrombophlebitis has sometimes been seen. The relationship of the skin lesions to mepacrine was suggested at an early stage. SENEAR *et al.* (1945) had reported skin lesions of a lichenoid type in a husband and wife who had used mepacrine as a suppressive for a considerable period ; while NOOJIN and CALLAWAY (1942) had incriminated mepacrine as the cause of an exfoliative dermatitis in a diabetic patient. DUEMLING (1945) also suggested that mepacrine was a causal factor in three cases of exfoliative dermatitis seen by him in the south-western Pacific area.

The arguments which have been put forward in favour of the view that mepacrine is a causal factor in this symptom complex are as follows :—

(1) The syndrome has been seen in all areas where large bodies of troops have taken mepacrine as a malarial suppressive.
(2) Those persons who have taken more than 0·7 gm. of mepacrine a week appear to have been more liable to develop the syndrome than those who have not exceeded this dosage.
(3) When in 1943, in the south-west Pacific area, the dose was increased to 0·7 gm. weekly, and discipline was enforced to see that this dose was taken, the incidence of the disease increased.
(4) Only 20 per cent. of those affected developed lesions within 3 months of beginning mepacrine therapy ; in 80 per cent. the lesions had developed in 7 months.
(5) Some, but by no means all, patients failed to improve until mepacrine was stopped.
(6) Re-administration of mepacrine caused a late chronic lichenoid reaction identical with the original lesions in 19·3 per cent. of cases (BAZEMORE *et al.* 1946).
(7) On experimental re-administration of mepacrine to 46 patients with lichenoid eruptions, exacerbations occurred in 9 ; in 6, the reinvolvement was extensive and in 3 only a few lesions were seen. The earliest relapse of lichenoid lesions occurred in 23 days and the longest in 97 days. In the majority of cases, the time of relapse was between 40 and 63 days. The exacerbations of atypical lichen planus on experimental re-administration occurred in the same frequency within three months as they had on initial ingestion of the drug (BAZEMORE *et al.* 1946).
(8) Lichen planus has occasionally been recorded after the long-continued administration of bismuth or arsenical preparations.

The evidence which suggests that mepacrine is not the primary factor in the production of the lichenoid eruption is as follows :—

1. The prevalence of atypical lichen planus was far greater in the south-western Pacific area among American troops than in other groups.
2. Many patients, despite lichenoid eruptions, continued to take 0·1 gm. mepacrine daily, but nevertheless improved.
3. Improvement took place when the patients were sent to Australia or the United States, but relapse occurred when they returned to the south-west Pacific area.
4. In 80·7 per cent. of patients, re-administration of mepacrine failed to produce a recurrence of lichenoid lesions.
5. In 37 out of 46 patients with lichenoid lesions, re-administration of mepacrine caused no exacerbation and most of the relapses occurred between 40 and 63 days after again taking mepacrine.
6. The application of mepacrine as a wet dressing did not increase the severity of the lichenoid lesions (EPSTEIN 1945).
7. It is stated by BUTLER (1947), but otherwise unconfirmed, that a similar disease was known to Filipinos before the war.
8. Attempts to demonstrate sensitivity, either by patch tests or by passive transfer tests, were unsuccessful in most of the patients who had lichenoid eruptions (PETERKIN and HAIR 1946, NELSON 1947).

It must, therefore, be confessed that the aetiology of the lichenoid eruption is still obscure. No fungi or bacteria of aetiological significance have been isolated, and attempts to demonstrate a virus by inoculation of biopsy material into embryonated eggs have yielded no results. It is possible, however, that a virus may have been the cause of the lichen planus, infection occurring only

in patients whose tissues have been made susceptible to it by previous administration of mepacrine, bismuth or arsenic.

The cause of the eczematous dermatitis, on the other hand, is simply a drug sensitivity similar to that described before the second world-war among those who had to handle mepacrine. Patch tests are as a rule positive in cases of this nature, while re-administration of mepacrine is followed by the reappearance of symptoms after a short interval. BECKER (1946), for instance, saw two patients who had recovered from eczematous dermatitis due to mepacrine in the Pacific area. When on leave in the United States, they developed attacks of malaria and were given therapeutic courses of mepacrine. Within 24 hours, both patients had developed skin lesions, in one instance urticarial, in the other of the vesiculo-bullous eczematoid type. HARVEY *et al.* (1944), working in New Guinea, reported an exacerbation of lesions in from 24 to 72 hours in 7 of 9 patients after administration of the drug. In each patient, the exacerbation was described as oozing or crusted and not of a lichenoid nature.

Thus, the mepacrine dermatitis complex contains at least two separate conditions: the eczematous dermatitis is due to drug sensitivity; in the aetiology of the lichenoid condition, mepacrine probably plays some part but its exact rôle is still uncertain. The eczematous dermatitis can occur and become extremely severe with small doses of mepacrine and at a very low plasma concentration. In this group, positive reactions to patch tests with mepacrine are to be expected. The second type is localized and morphologically resembles lichen planus. Prolonged administration of the drug is apparently necessary to elicit this reaction. In this connexion, it may be of interest to note that FORMAN (1947) has recently emphasized the frequency with which lichenification of the skin is associated with anxiety states and hysterical traits or with depression.

Treatment of skin lesions.—The treatment of the lesions associated with the mepacrine dermatitis complex is unsatisfactory. Mepacrine must be stopped, although in some patients no improvement may occur until they have stopped taking the drug for 2 or 3 months. Some patients who ceased to take mepacrine failed to improve till penicillin had been administered. Neither thiobismol, arsenical preparations nor large doses of vitamin A caused any improvement (BAZEMORE *et al.* 1946). WILSON (1946) believed that deficiency of vitamin A was a predisposing cause; while in view of the fact that lesions similar to those of riboflavin deficiency may be seen, and that mepacrine may possibly interfere with the metabolism of riboflavin, large doses of vitamins of the B complex, as recommended by BERESTON and CHENEY (1946), and more especially of riboflavin, may be of value. Many of the patients who suffered from skin lesions due to mepacrine in the Pacific area are said by BUTLER (1947) to have been living on a diet deficient in fresh vegetables, milk and meat. Other observers, however, state that the diet was excellent (ROSENTHAL 1946). It may be noted that as SCUDI and HAMLIN (1944) and FITZ-HUGH *et al.* (1945) have pointed out a high protein, low fat diet reduces the toxicity of mepacrine in rats, especially in relation to the extent of the liver lesions. Bland non-irritating solutions such as 1 : 9000 potassium permanganate solution soaks may be of value. Sulphonamide ointments, tincture of iodine and mercurial ointments should be avoided. As some patients appear to be sensitive to light, exposure to sunlight must be avoided.

It would be interesting to know whether any persons who have developed lichenoid lesions while taking mepacrine subsequently show a recrudescence of the lesions after prolonged therapy with either bismuth or arsenical preparations.

(ii) *Toxic psychoses.*

Very shortly after mepacrine had been introduced, reports began to appear of toxic psychoses and other nervous phenomena which were attributed to its use. In some cases, as in those described by CHOPRA and ABDUL WAHED (1934), DECHERD (1937), CHOREMIS and SPILIOPOULOS (1938), and AYALA and BRAVO (1942), mepacrine had been combined with pamaquin and there was some uncertainty whether the nervous symptoms were due to one or other of these drugs or to their combination. KINGSBURY (1934), however, with two years' experience in Malaya, was able to collect 12 cases; others were added by GREEN (1934 a and b). One case was reported from India by GOVINDASWAMY (1936) while from China, KANG and JARVIS (1936) recorded one case and WILKINSON (1939) three others. The malarial epidemic in Ceylon, when soluble mepacrine (atebrin musonate) was extensively used intramuscularly, in addition to mepacrine by mouth, provided a considerable number of cases (BRIERCLIFFE 1935, UDALAGAMA 1935, HAY *et al.* 1935). Reports before 1939 had rather suggested that mepacrine psychoses were more common among members of Eastern races than among those of European extraction. ALLEN *et al.* (1937), however, reported 9 cases among persons given therapeutic malaria in America, BISPHAM (1936 and 1941) observed one case, and LERRO (1941) in Panama also recorded a case. SHEPPECK and WEXBERG (1946) subsequently described 19 cases seen between 1935 and 1943 in the Gorgas Hospital, Panama.

The incidence of psychoses due to mepacrine is extremely low as is shown in Table II. It will be seen that the numbers tend to be highest among those who were given malaria therapy for cerebral syphilis and subsequently treated with mepacrine, as well as among those groups where soluble mepacrine was given intramuscularly. Among specially selected persons, such as European troops in West Africa, the incidence was extremely low in those treated with

TABLE II.

The Incidence of Nervous Reactions following Administration of Mepacrine.

No. of persons given mepacrine	No. with nervous involvement	Incidence per 1,000 cases	Observers
30,000	35	1·16	LIDZ & KAHN (1946)
20,000	2	0·1	NIETO-CAICEDO & GUERRERO (1946)
11,584	3	0·25	FINDLAY (1947)
9,000	4	0·44	HOOPS & BARROWMAN (1938)
7,604	35	4·6	GASKILL & FITZHUGH (1945)
4,876	19	3·9	SHEPPECK & WEXBERG (1946)
1,628	6	3·6	FIELD (1938)
1,207	1	—	HOOPS (1935)
750	2	2·66	GREEN (1934)
† 644	7	10·8	UDALAGAMA (1938)
500	0	0	FIELD (1938)
422	1	2·3	BISPHAM (1938)
450	4	8·8	VOLLMER & LIEBIG (1944)
* 300	5	16·6	READ *et al.* (1946)
† 203	2	9·8	FIELD (1938)
Totals 89,168	126	1·4	

* Therapeutic malaria for neurosyphilis.
† Soluble mepacrine and mepacrine *per os.*

therapeutic courses of mepacrine, while among approximately 30,000 Europeans taking 0·1 gm. mepacrine from March 1943 to March 1946 there were no cases of toxic psychosis. The high incidence reported by UDALAGAMA (1935) in Ceylon, may be due to the fact that he included all states of depression following mepacrine administration ; these may or may not have been due to the drug.

Mepacrine psychoses usually, though not invariably, begin after the fever has subsided and parasites have disappeared from the blood stream. Symptoms have been noted as long as 12 days after cessation of mepacrine therapy, but the interval is usually shorter. GASKILL and FITZ-HUGH (1945) found the onset most common 6 days after treatment had ended, though some patients developed symptoms on the third day after having taken 0·9 gm. by mouth. SHEPPECK and WEXBERG (1946), in their series of 19 cases, found that the average interval between the disappearance of fever and the onset of psychosis was 2·2 days, the median 2 days ; the average interval between the disappearance of parasites and the onset of psychosis was 2·6 days, the median 2 days. BRIERCLIFFE (1935) noted that when mepacrine was given by mouth, mental symptoms usually began at the end of 5 days ; with intramuscular injections the onset would be shortly after the first or within 24 hours of the second injection.

The symptoms associated with mepacrine psychosis vary. States of manic or hypomanic excitement with euphoria are most common. Probably those cases labelled " cerebral " excitation by some of the earlier observers fall into this group. Some patients become so stimulated mentally, that they write poems, compose music or paint pictures. Delirium, visual hallucinations combined with an otherwise catatonic condition, schizophrenic-like symptoms, paranoid syndromes and acute confusional states have all been reported, while depression, and in one instance prolonged coma, have been noted (BECKMAN 1942). Women may suffer from sexual excitement and delusions of having been raped. Disorientation as to time, place and person is not uncommon, while a fine tremor has been observed (MERGENER 1945). The mental integration of the patient would seem to be of importance in determining the type of psychotic reaction, though it may not have anything to do with initiating the condition.

The onset is usually sudden, but in a few cases it may be preceded by a short period, a day or less, of nervousness, malaise, restlessness or insomnia. When the onset is insidious loss of memory for recent events may be well marked, the patient becoming withdrawn and secretive. The psychosis develops rapidly to a climax within a day, or even less, and remains at its height for a period varying from one day to five weeks. As a rule there is rapid subsidence of symptoms. SHEPPECK and WEXBERG (1946) found the average duration of symptoms to be 8·5 days, the median 2·5 days. The outcome is very generally complete recovery, but there may be difficulty in concentrating or in remembering for some time, while the speech is rather slow. In the series of cases recorded by GASKILL and FITZ-HUGH (1945), 33 of 35 cases completely recovered in from 8 to 85 days, the average being 23 days. Two patients who developed schizophrenia did not recover. Some fatal cases have been recorded. One patient, while in a state of profound depression, committed suicide (NIETO CAICEDO and GUERRERO 1946). In another instance, a fatal psychosis developed after 2·4 gm. mepacrine had been given to a patient who was apparently suffering from undiagnosed dementia paralytica. A third patient, after receiving 3 gm. of mepacrine, developed a subacute toxic delirium, associated with fever, two days later : death took place with hyperpyrexia after a further 13 days.

There is no constant relationship between the dose of mepacrine and the liability to develop symptoms, since toxic psychoses have been seen after

as little as 0·5 gm. SHIERS (1946), for instance, reported a case of marked cerebral excitement after very small doses, the attacks returning whenever mepacrine was given. WHITMAN-NEWELL and LIDZ (1946) believe that mepacrine psychoses rarely occurred when doses not exceeding 2·8 gm. were given as treatment in 7 days. When massive dose schedules became popular later, the incidence of toxic psychoses increased. LIDZ and KAHN (1946) found that psychoses were not uncommon when 3·8 to 4·8 gm. were given in 7 days or 1·4 gm. in 24 hours. This is in agreement with the finding of the Malaria Commission of the League of Nations (1937), who believed that the incidence of psychoses increased with large doses, with the length of the period over which mepacrine was given, and with the use of atebrin musonate. ALLEN *et al.* (1937) suggested that a relationship existed between the dose of mepacrine per kgm. of body weight and the duration of symptoms. The correlation, however, is not very exact, for while 4 patients who took more than 25 mgm. per kgm. of body weight had symptoms of over 10 days' duration, 2 patients who had symptoms lasting more than 10 days had taken only 19·1 and 24·1 mgm. per kgm. of body weight. GASKILL and FITZ-HUGH (1945) gave mepacrine to 16 patients who had recovered, without untoward result in 15 ; one patient became mildly excited. In the case reported by SHIERS (1946) the symptoms returned when mepacrine was readministered.

Very rarely, and particularly in small children, acute forms of polyneuritis or myeloradiculoneuritis have been ascribed to the taking of mepacrine. Two cases have been described in Italians (MOSCHINI 1935 and VALENTINI 1937) and six in Greek children by CHOREMIS and SPILIOPOULOS (1938), associated with polyneuritis and paralyses of the lower limbs. It must be remembered that a very similar neurological picture has been recorded in patients suffering from malaria and treated with quinine ; the question therefore arises whether mepacrine is the main factor in the aetiology of the polyneuritis. In the case of an adult treated with mepacrine LERRO (1941) observed paraesthesia over the whole body, nausea, vomiting and a choking sensation. Epileptiform fits are reported by VARDY (1935), FIELD and NIVEN (1936) and SIEGENBEEK VAN HEUKELOM and OVERBEEK (1936), a matter of some interest, as, according to MOLITOR (1941) clonic convulsions are produced in animals by large doses of mepacrine. VAN SLYPE (1936) observed three cases of convulsions in children and one case of bulbar paralysis with flaccid paralysis of the lower extremities.

Very little is known of the mechanism by which mepacrine brings about these nervous lesions. Riboflavin deficiency is not associated with nervous phenomena, so that a sudden interference with riboflavin metabolism by mepacrine is not a probable cause. As the African diet is very often deficient in riboflavin, the administration of mepacrine to Africans should result in a high incidence of psychotic reactions if this theory were correct : this certainly was not noticeable among African soldiers treated with mepacrine. The symptoms are not those of cerebral malaria nor do they bear any relationship to a Herxheimer reaction, which might equally be due to destruction of malarial parasites by other antimalarial drugs. It seems probable therefore that the psychosis is due to a direct interference with the metabolism of the nerve cell by mepacrine. In animals, HECHT (1933) found evidence of cerebral stimulation after lethal doses. MOLITOR (1941) states that, occasionally, high concentrations of mepacrine are found in the cerebrospinal fluid ; but no mepacrine was present in the cerebrospinal fluid of the patient with acute poisoning described by MARKSON and DAWSON (1945). Certain experiments by MANIFOLD (1941) are of interest in this connexion. Various acridine dyes not, however, mepacrine were tested for their action on the carbohydrate and pyruvate oxidation systems of brain tissue *in vitro*. Acriflavine was found to inhibit oxidation in high concentration, the action suggesting a breakdown in carbohydrate metabolism

similar to that found in the absence of aneurin; this provides a possible explanation for a certain similarity between the psychiatric pictures caused by mepacrine and by a deficiency of aneurin. LIDZ and KAHN (1946) have suggested that mepacrine may produce mental impairment, without actual psychosis, whenever the serum levels are above 18μgm. per 100 ml.: this was judged by scores on the Kohs Block test, in which the mental age is assessed by forming standard patterns with coloured cubes. Thus doses of 2·1 gm. in 7 days were without action in causing impairment of the mental faculties while 4·5 gm. in 6 days caused a very definite impairment.

It would thus seem that mepacrine psychoses are likely to develop only if the plasma or serum levels are allowed to remain at a consistently high level.

The diagnosis of mepacrine psychosis usually presents little difficulty. ALLEN (1944), however, has drawn attention to a case where the euphoria and delusions of grandeur caused a diagnosis of general paralysis to be made. It should be remembered in this connexion that a recent attack of malaria may cause false positive Kahn and Wassermann reactions.

The value of any particular treatment in mepacrine psychoses is difficult to assess, since in so many patients the symptoms subside spontaneously. Treatment similar to that used in alcoholic psychoses has been suggested by SHEPPECK and WEXBERG (1946): this consists of aneurin hydrochloride 50 mgm. intravenously four times a day, aneurin hydrochloride tablets 10 mgm. and nicotinic acid 50 mgm. three times a day, and two compound vitamin B capsules three times a day by mouth, each capsule containing 5 mgm. aneurin hydrochloride, 25 mgm. riboflavin and 25 mgm. nicotinamide. It should, however, be noted that in rats HEGSTED *et al.* (1945) found that mepacrine retarded the onset of vitamin B_1 deficiency. In addition, fluids are given in large quantities and the bowels are kept open. The effects of large doses of riboflavin alone would be of interest, while glucose intravenously might be of value since it is known that soluble mepacrine given intravenously reduces the blood sugar.

(iii) *Haematopoietic lesions.*

In rare instances, aplastic anaemia, agranulocytosis and acute hepatitis have been seen in association with either the lichenoid-eczematoid syndrome or with exfoliative dermatitis. Similar blood changes have also occurred in those taking mepacrine, in the absence of skin lesions. CUSTER (1946) found that in the United States Army the case incidence of aplastic anaemia in areas where mepacrine suppression was in force rose during the years 1943 and 1944 from 0·66 to 2·84 per 100,000 compared with a case incidence of 0·04 to 0·18 in other theatres of war. In 47 cases of aplastic anaemia occurring in those who had taken mepacrine, the period of mepacrine suppression varied from 1 to 34 months. The mepacrine dermatitis complex preceded the aplastic anaemia in twenty cases, but the dermatological therapy employed was not a significant causal factor. The pathological findings were typical of those found in aplastic anaemia. Liver lesions were found in 10 patients at necropsy; in 5 these hepatic lesions were indistinguishable from those seen in infective hepatitis. The haematological features were essentially those of normocytic, normochromic anaemia with leucopenia and thrombocytopenia. Reticulocytes were usually very scanty. A haemorrhagic tendency was frequently noted early, while the subsequent course was almost invariably marked by fever and haemorrhagic phenomena. Four out of 47 patients survived for periods varying from 2 to 7 months. ROSENTHAL (1946) has also described two cases of aplastic anaemia in association with the lichenoid dermatitis. One patient recovered, while the other died. At necropsy, apart from widespread petechial haemorrhages, there was chronic focal myocarditis: the liver showed oedema, periportal degeneration

of the parenchyma and infiltration by lymphocytes and fibroblasts, with localized masses of pigment mostly within macrophages in the periportal regions. The pigment gave a reaction for melanin with Becker's stain. A few cases of agranulocytosis have also been recorded. Treatment is unsatisfactory.

When large doses of mepacrine of the order of 50 to 200 mgm. per kilo of body weight daily were given to rats, mice, rabbits, hamsters, guineapigs, dogs, monkeys, chickens and ducks, peculiar basophilic inclusions, usually associated with vacuoles, appeared in the cytoplasm of lymphocytes. Inclusions of a similar nature occurred in the erythrocytes of the rat, mouse and hamster, and rarely in the monocytes of the rat. Anaemia, "polynucleosis", lymphopenia and monocytosis occurred in the rat, while "polynucleosis" and lymphopenia developed in other species. The nature of these inclusions is unknown, but they do not appear to be parasitic in nature (MUSHETT and SIEGEL 1946) and nothing like them has been seen in man. RUSSELL (1945) has described an eosinophilia in man as the result of prolonged mepacrine administrating. This finding has not been confirmed and was probably due to other causes.

(iv) *Ophthalmological changes.*

A new industrial hazard has been found to occur among those engaged in handling mepacrine in large quantities. Reference has already been made to the occurrence of skin eruptions on exposed parts of the body, puffiness of the eyelids, lachrymation and pain over the frontal sinuses. MANN (1947) has now described a curious corneal condition in 6 male workers handling mepacrine; all had pigmented yellow skin. The patients worked for short periods without goggles, masks or protective clothing in an atmosphere which contained clouds of very fine mepacrine dust. They had no dermatitis, but the conjunctivae also were yellow. After working for some weeks, they all noticed that at night a point source of light had a blue halo round it. One yard (0·9 m.) away the halo began 2 in. (5 cm.) from the source and was about 3 in. (7·5 cm.) wide. It was dark blue at the inner edge and pale blue at the outer edge. At a distance of 6 yards (5·4 m.), faint yellow, green, and reddish-brown bands appeared outside the blue ring. All the men had normal visual acuity.

On slit-lamp examination, the condition of all patients was similar. There was yellow discoloration of the conjunctiva in the interpalpebral space, and a slight dulling and yellowing of the cornea which was barely visible macroscopically. Under magnification there appeared to be an actual deposit of minute dark-brown dots at the exposed margins of the limbus. The whole surface of the cornea was peppered with very fine dust-like particles, which appeared dark yellowish-brown by direct illumination and opaque by transmitted light. The size of the particles was estimated as between 5 and 10 μ in diameter—that is, about the size of the nucleus of a corneal epithelial cell. The corneal surface was perfectly smooth and bright, and the change was present only in the surface layer of cells. In the lower part of each cornea there was a series of wavy yellow lines which were composed of closely aggregated dots, similar to those peppered over the cornea, but closer together and of a bright yellow colour. One patient noticed the haloes after being employed for less than a year; they disappeared within 2 months of a transfer to a different job. Later, he returned to work with mepacrine and the phenomenon reappeared in 6 months, although it did not reach its previous intensity. There was no evidence of glaucoma in any of the patients, and it seems reasonable to attribute the condition to a diffraction effect.

Two male volunteers, who had both taken 100 mgm. of mepacrine by mouth daily for 7 months, showed a pale-yellow staining of the skin generally, but their eyes were normal and they had never seen blue haloes. Mepacrine dust blown directly on to the eyes of rabbits produced in 6 days an appearance on

slit-lamp examination similar to that seen in human subjects. These observations suggest that the corneal condition is caused by direct contamination with mepacrine dust. The particles seen may not be mepacrine itself, since this is soluble in the tears, and the exact nature of the precipitates is doubtful, although they are probably an insoluble breakdown product of mepacrine. Histological examination of an affected rabbit's eye was carried out, and the yellow granules in the cytoplasm could be seen in unfixed specimens. They were very small and amorphous. The opaque yellow dots seen with the slit-lamp are the whole aggregation of these amorphous particles within the cell containing them. It was suggested that they might be composed of 2-chloro-7-methoxyacridone—an insoluble substance which is formed by hydrolysis of mepacrine.

An additional toxic effect on the eyes has been noted by REESE (1946) who saw three patients suffering with oedema of the corneal cells as a result of taking large doses of mepacrine. Blurring of vision was noted in both eyes and examination with a slit-lamp showed " bedewing " of the cornea due to the presence of isolated points of oedema. One patient had taken 0·2 gm. for 27 days, while the others had had high therapeutic doses combined with suppressive mepacrine. When mepacrine was stopped, the oedema disappeared but recurred when the drug was re-administered. CHAMBERLAIN and BOLES (1946) similarly recorded four cases : three of their patients had taken mepacrine for only four to six weeks in doses of 0·1 gm. daily before blurring of vision came on. In one instance, the visual acuity was as low as 1 : 200 in each eye and in all the patients some degree of hepatic dysfunction was noted. The corneal opacities were for the most part situated near the level of Bowman's membrane.

It is estimated that at least 25 cases of this type occurred in the Pacific theatre.

Mepacrine and Blackwater Fever.

The question whether mepacrine therapy precipitates an attack of blackwater fever is of some interest. It has long been recognized that quinine may be a precipitating factor, while pamaquin is also known to give rise to methaemalbumin in the blood and, if this is formed in sufficient amounts, to the escape of haemoglobin products through the kidney into the urine. Many cases have been recorded where the administration of a combination of pamaquin and atebrin has been followed by haemoglobinuria (BANERJEE and BRAHMACHARI 1933 ; AMY 1934 ; NAUMANN 1934a ; MOIR 1934 ; MURRAY 1934 ; and CHOPRA and CHAUDHURI 1935). NÄGELSBACH (1933), however, recorded the case of a woman in labour who developed blackwater fever while taking mepacrine ; in some of the cases recorded by NAUMANN (1934b), the patients had mepacrine only ; FOY and KONDI (1937) reported 3 cases of blackwater fever where mepacrine had been given but quinine had not been taken for at least three months, while GUNTHER (1938) also described one case where blackwater fever appeared to be precipitated by the administration of mepacrine. It is noticeable that the blackwater fever developed as a rule either after very small doses of mepacrine, in one instance 0·4 gm. in 48 hours, or after the completion of what would now be regarded as an inadequate dosage (1·5 gm. in 5 days) for the treatment of an attack of malaria.

HOOPS (1935) found that the use of mepacrine in a labour force in Malaya reduced the incidence of blackwater fever. The experience of FINDLAY and STEVENSON (1944) in West Africa was similar : among European troops the introduction of mepacrine as a suppressive, 0·6 or 0·7 gm. weekly, with mepacrine only in the treatment of malarial attacks, 0·8 gm. being given in the first twenty-four hours, completely abolished blackwater fever.

SIEGEL and MUSHETT (1944) found that a massive haemoglobinuria could be produced in young rats, only by giving massive doses far in excess of those ever

given to man therapeutically. It thus seems that mepacrine is far less likely to precipitate blackwater fever than is quinine.

To concentrate entirely on its toxic reactions is obviously to give an entirely false picture of the results obtained with mepacrine in the treatment and prevention of malaria, for during the war mepacrine was given without ill effect to hundreds of thousands of persons in the services. While it would be an exaggeration to say that mepacrine won the war in the East, there is no doubt that without its aid the sickness rates would have been much higher, the deaths would have been far more numerous and ultimate victory would have been long delayed.

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SUMMARY OF RECENT ABSTRACTS.*

VII. HELMINTHIASIS.

[*Continued from p.* 691]

Nematodes.

Hookworm infestation etc.—SANGSTER (p. 759) reports cases of hookworm infestation in Australian soldiers in New Guinea and Bougainville. Ground itch, cough, sore throat, blood-stained sputum, abdominal discomfort, nausea, diarrhoea and anaemia were observed in various patients. Three men had severe and acute illness, with anaemia and persistent bloody diarrhoea. Both *A. duodenale* and *N. americanus* are found in Bougainville, but only the latter in New Guinea. In American soldiers with hookworm infection, ROGERS and DAMMIN (p. 1049) noted that the prominent symptoms were gastro-intestinal (nausea, vomiting, epigastric pain, diarrhoea) with eosinophilia (up to 70 per cent.) but without anaemia. Direct stool examination was positive in only half the patients, but zinc sulphate floatation was effective. Routine treatment was with tetrachlorethylene.

GELFAND (p. 1049) discusses the clinical features of hookworm disease in Africans (in whom anaemia is relatively frequent) and in Europeans (in whom it is not, but in whom abdominal pain and flatulence are common). He thinks that there is some element of toxaemia in hookworm disease.

DICK and MCCARTHY (p. 660) point out that anaemia does not occur in hookworm infestation if the diet is plentiful and good. Their investigations were made in East African soldiers. CRUZ and DE MELLO (p. 660) make the same point, with emphasis on the iron content of the diet ; they have therefore experimented with various iron salts to be included in food. SCOTT (p. 1050) makes the point that hookworm infestation produces anaemia only in persons whose haematopoietic system is near the limit of its power of compensation, as a result of malnutrition. In examinations of schoolchildren in Georgia, U.S.A., the anaemic were checked by haemoglobin estimations, and egg counts were made. In severe cases the families were visited, and affected persons were treated. The sanitary control programme, which is the final solution of the hookworm problem, has not yet reached the whole population. Hookworm infection has greatly diminished in Texas during the past 30 years. SCOTT (p. 465) thinks that this is due partly to control programmes, and partly to the improvement in economic status which has taken place.

STUBENBORD and ALLEN (p. 1050) report two fatal cases of hookworm disease in infants.

HERNÁNDEZ MORALES and DIAZ RIVERA (p. 230) describe three cases in which severe symptoms of poisoning occurred after the ingestion of a mixture of 2 cc. carbon tetrachloride and 1 cc. oil of chenopodium. The patients were adult males ; all recovered. MUKERJI and SEN GUPTA (p. 230) show that oil of chenopodium should be stored in a cool place (not above 75°F.) and should be protected from direct light ; otherwise, the ascaridole content decreases.

HUNTER and WORTH (p. 567) exposed two volunteers to large numbers of filariform larvae of *Ancylostoma caninum*. The reactions, which were very different, are described.

FISCHER (p. 465) describes in detail the clinical history of a patient infected with *Strongyloides stercoralis* ; diarrhoea and abdominal pain were marked, and

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1946, v. 43. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

eosinophilia reached 80 per cent. Larvae were found in the stomach contents and bile, and eggs in the latter; larvae were also found in the faeces, but never eggs. Gentian violet was not successful in treatment, but neither were most of the other drugs employed. LAPTEV (p. 50) reports a case of *Strongyloides* infection of the lung, in which mature worms were found in the sputum. The condition cleared up after treatment with alcohol intravenously, and methylene blue by the mouth. DA SILVA (p. 1158) notes that infestation with *S. stercoralis* is fairly common in part of Brazil—he has found infestation in 30 per cent. of people examined by duodenal intubation. He claims that the best results in treatment are attained by the introduction by duodenal tube of 20 cc. of a 0·1 per cent. solution of gentian violet, or by capsules of 0·025 gm. given twice a day.

Ascariasis etc.—MILWIDSKY (p. 568) describes the surgical complications of ascariasis, the most common of which is intestinal obstruction. YANG and LAUBE (p. 661) give an account of 19 cases of biliary ascariasis; the symptoms suggested cholecystitis. DROUET *et al.* (p. 467) report a case in which haemorrhage occurred into the vitreous humour of the eyes, which they attribute to the toxic action of *Ascaris*, giving their reasons for this opinion.

ROCHA E SILVA and his collaborators (p. 1052) have studied the mechanism of shock induced in dogs by the injection of an extract of *Ascaris*; they conclude that this form of shock, and anaphylactic shock, have the same mechanism. This work is complicated, and the account should be read in original.

ALEXANDER and TRIM (p. 569) have investigated the biological activity of surface active substances (sodium cholate etc.) on the penetration of hexyl resorcinol into *Ascaris*. For details the original should be consulted.

HILMY (p. 51) has shown that a method of drying liquid sludge, and scum from sedimentation tanks, which has been introduced in Egypt, is effective in destroying the eggs of *Ascaris*, except during the period from December to March, when for climatic reasons the ordinary piling method is preferable. For detail, the original should be consulted.

VISHNIEVSKAYA (p. 565) has made a study of the worm eggs found in sewage water used for the irrigation of fields in the Kharkov district. Eggs of several species were found, but the results are related to those of *Ascaris*, which were present in large numbers and of which a large number were morphologically unchanged. *Ascaris* eggs were found on vegetables as well as in the soil. ALF (p. 566) failed to find eggs of *Ascaris* in soil more than 0·5 metre from the wall of a pit containing heavily contaminated faeces, or more than 1 metre below the floor of the pit.

SEN and GHOSE (p. 576) describe probably the first recorded case of *Gnathostoma spinigerum* in the human eye.

Filariasis.—FLOCH and DE LAJUDIE (p. 352) found microfilariae of *Wuchereria bancrofti* in 12–18 per cent. of people in French Guiana.

WEBSTER (p. 575) shows that about half of 80 white people, who had lived many years in Samoa, had symptoms and signs of filariasis; many of them had elephantiasis. Most had not been exposed to infection until they were 30 years of age.

SCHLOSSER (p. 575) found *W. bancrofti* in about 20 per cent. of inhabitants of the Solomon Islands; the microfilariae showed definite nocturnal periodicity. [In the abstract of this paper the mosquitoes *Anopheles punctulatus punctulatus* and *Anopheles punctulatus farauti* are referred to as *Aëdes*. In the original paper the author refers to them only as *A. punctulatus punctulatus* and *A. punctulatus farauti*; it would have been wise to give the full names at least once in the course of the paper.]

KARTMAN (p. 760) found infection with *W. bancrofti* in 2–18 per cent. of *Anopheles funestus*, and in 28–54 per cent. of *A. gambiae* in the neighbourhood of Dakar.

NEWTON *et al.* (p. 52) have allowed mosquitoes of 16 species indigenous to America to bite volunteers infected with *W. bancrofti*. Of these, *Culex quinquefasciatus* [*C. fatigans*], *C. tarsalis*, *Psorophora confinnis* and *Anopheles albimanus* would be excellent vectors under favourable conditions, and three other species would be rather poor vectors.

NEWTON and PRATT (p. 52) have shown that infective larvae of *W. bancrofti* are capable of migrating from the abdomen to the proboscis of a mosquito. They conclude that infective larvae occurring anywhere in the body of a mosquito are potentially capable of infecting man.

RAO (p. 231) found filarial infection only in *Mansonioides annulipes* [=*longipalpis*] in a village in Central Provinces, India, in which *W. malayi* was discovered.

MICHAEL (p. 53) has given a detailed description of the pathological changes which occur in filariasis due to *W. bancrofti*. These may be allergic and transitory, the effects of sensitization, or they may be the result of the presence of the worm, and consist of thickening and degeneration of the endothelium of lymphatic channels, with lymphangitis oedema, infiltration, fibrosis, and varicosity. These lesions are essentially the tissue changes associated with all infectious granulomata, plus those due to foreign body irritation. Examination of the blood is not enough for diagnosis ; the method of choice is laboratory examination of biopsy material.

ROSE *et al.* (p. 232) produce evidence which suggests that lymphangitis in the course of filariasis is an allergic phenomenon, and that secondary streptococcal infection is of little or no aetiological importance.

WOLFE and SCHOFIELD (p. 762) found living *W. bancrofti* adults in a greatly dilated lymphatic vessel in the spermatic cord of an American serviceman who had been stationed in tropical Africa.

DHAYAGUDE (p. 353) reports further cases of microfilarial granuloma of the spleen ; from some of the specimens, living microfilariae were obtained, which were *W. bancrofti*.

RIFKIN and THOMPSON (p. 353) describe the pathology of filariasis. Three stages are recognized :—the stage of local or general allergic reaction ; the subacute stage characterized by proliferative granulation tissue in the lymphatic tissues harbouring the parasite ; the late chronic stage of non-specific fibrous tissue overgrowth.

THOMPSON, RIFKIN and ZARROW (p. 468) give a detailed description of the clinical and pathological features of the early stages of filariasis, recognizing 3 stages :—(1) The *early acute phase* of sudden lymphangitis and soft swelling of the glands ; no microfilariae are found in the blood. (2) the *subacute phase*, without lymphangitis or swelling, but with some aching of the part, and proliferation of the walls of the lymphatics and of the glands. (3) The *early chronic phase*, again without microfilariae in the blood ; there is chronic swelling and generalized reticulo-endothelial hyperplasia with irregular fibrosis. These changes refer to early filariasis ; the account should be read in the original.

SAPHIR (p. 54) has studied the early clinical manifestations of filariasis in a series of patients in whom the diagnosis could not be confirmed by the finding of microfilariae. Early aching pain in the limbs was followed by recurring attacks of pain in axilla, arm, groin, thigh or scrotum, sometimes accompanied by swelling. The glands became enlarged and tender, and lymphangitis occurred.

BEHM and HAYMAN (p. 762) discuss the diagnosis of filariasis in American troops who have been stationed in the endemic area ; they rely chiefly on clinical diagnosis, especially a history of one or more attacks of *mumu* (fever,

lymphadenopathy and retrograde lymphadenitis), and state that the intradermal test with antigen from *Dirofilaria immitis* gives too many false positives in uninfected persons, to be useful. Adenopathy alone is of little significance, since it was extremely common in the troops in the Pacific. A similar account of the same patients is also given by BROWN *et al.* (p. 939).

LEEDE and JOSEY (p. 573) discuss the early diagnosis of filariasis, much on the same lines as other authors mentioned in this Summary.

HARRIS and SUMMERS (p. 569) describe a concentration method for microfilariae in the blood, which involves the use of heparin, saponin, and the centrifuge.

OLIVEIRA (p. 940) discusses the surgical aspects of elephantiasis.

OLIVER-GONZÁLEZ and MORALES (p. 471) have prepared antigens, for skin tests in filariasis, from microfilariae of *W. bancrofti* and from *Ascaris* and *Necator*. They found evidence of a group reaction, and that persons with other nematode infections gave positive results, as well as those with filariasis, so that the test is useful only when other nematode infections are absent.

ZARROW and RIFKIN (p. 571) prepared an antigen from *D. immitis* and used it for a skin test for filariasis. They state that in a dilution of 1 in 4,000, positive results due to intestinal worms are not given, but that in filariasis the test was positive in a great majority of cases. Full details must be sought in the original.

GOODMAN *et al.* (p. 573) discuss diagnosis and progress of filariasis in American soldiers. Skin tests with antigens from *D. immitis* and *Setaria equina*, diluted to 1 in 8,000, were positive in just over half the cases, but some controls were positive to this and to a complement fixation test. Microfilariae in the blood were found very rarely. Prognosis is good. WHARTON and STELMA (p. 1054) find that with an antigen prepared from *D. immitis*, and used in a dose of 0·01 ml. of dilution 1 in 8,000, there are some false positive results in persons not infected with filariae, and, on the other hand, that with a dilution of 1 in 100,000, only 80 per cent. of infections are detected. The paper should be read in full.

WARREN *et al.* (p. 1056) found that complement-fixation tests with sera from persons in whom the clinical diagnosis of filariasis had been made, with antigen prepared from microfilariae of *W. bancrofti*, were negative, although similar tests with antigen from adult *D. immitis* were strongly positive. Intradermal tests were positive in about two-thirds, with each antigen. From cross-immunity tests, the authors conclude that each of these filarial species contains a species-specific, and also a group-specific, antigen.

AUGUSTINE and LHERISSON (p. 570) think that, in some parts of the world, man may be constantly exposed to infection with filarial nematodes carried by biting insects, but not pathogenic for man, and that these may create, in man, a reaction of immunity which complicates reactions to tests in which the antigen is prepared from *D. immitis*. They quote experimental work in support of this contention.

CULBERTSON *et al.* (p. 54) have treated a few patients, in whose blood microfilariae were found, with Neostibosan for periods up to 48 days. The results were promising, though by no means strikingly good. CULBERTSON *et al.* (p. 354) report further on patients treated with Neostibosan and observed for a year; 13 of 30 had remained free of microfilariae, and in five the numbers were greatly reduced. In controls the infection had not diminished in the same period. In a later report (p. 763) they show that 20 of 35 treated persons lost all filariae in 15 months, and in others the numbers were much reduced. Controls showed no reduction.

LAWTON *et al.* (p. 55) report the results of treatment of dogs infected with *D. immitis*, and cotton-rats infected with *Litomosoides carinii*, with preparations of mercury and antimony. Some of the latter showed activity against the worms.

ASHBURN *et al.* (p. 662) have examined *D. immitis* from dogs given treatment with antimony preparations. The drugs apparently caused changes in the ovary, the developing ova and the larvae, which ensured at least temporary sterilization of the female worms.

On the assumption that lymphangitis in filariasis is associated with allergy, PRATT (p. 470) has used adrenaline in treatment, with some success in relieving symptoms.

COGGESHALL (p. 852) notes that, in 1942, more than one-quarter of the United States marines in the Samoan area became infected with *W. bancrofti*. He emphasizes the fact that the early symptoms—lymphangitis, lymphoedema and lymphadenopathy—are unlike the usual descriptions of the disease as it is seen in the Samoan people, and he stresses the fact that the signs disappear if the patient is removed from the chance of reinfection. Filariasis cannot establish itself in the United States.

In a study of the psychosomatic aspects of filariasis in American troops, ZELIGS (p. 53) concluded that the disease soon dies out after the patient is removed from the endemic area, that rehabilitation is best obtained by a combined programme, that no impairment of sexual functions has resulted from filariasis, and that severe sequelae have occurred in only 0·2 per cent. of cases. BUCHANS (p. 231) stresses the fact that elephantiasis occurs only in persons subjected to constantly repeated infection over a period of years. MCMARTIN (p. 231) also writes, in reassuring fashion, that permanent disability due to filariasis will be rare in the United States troops who served in endemic areas. He gives indications for treatment of filariasis.

WILLIAMS and BROWN (p. 663) show that the filarial worm *Litomosoides carinii* is transmitted in cotton rats (*Sigmodon hispidus*) by the tropical rat mite (*Liponyssus bacoti*).

Onchocerciasis etc.—WANSON and HENRARD (p. 232) describe the life-history of *Simulium damnosum*; they note that adult females migrate to villages, from the watercourses, to a distance of several miles (45 is the maximum quoted). WANSON *et al.* (p. 233) show that in fishermen living near rivers, in the Belgian Congo, in which *S. damnosum* breeds, the rate of infection with *O. volvulus* may be 100 per cent., and that in villages 5 miles away the rate may be 65 per cent. Near the rivers 15 per cent., and 5 miles away 3 per cent., of the flies were infected. *S. damnosum* is the only known vector in this area.

RIDLEY (p. 55) refers to the large amount of blindness which, in Africa, is due to onchocerciasis. In 300 persons examined for the disease, in the Northern Territory of the Gold Coast, 136 were found infected, and of these, 22 were blind or almost blind, and visual defects were present in 51. This was probably not a representative group of people. The author makes the point that ocular defects which are sometimes attributed to trypanosomiasis may often be due to onchocerciasis. PACHECO-LUNA (p. 1159) states that on the slopes of the Sierra Madre in Guatemala, about 20,000 people suffer from onchocerciasis, of whom one-third show ocular manifestations, and 2 per cent. are blind. He gives a detailed account of the pathology of the ocular conditions, which should be read in full. PUIG SOLANES *et al.* (p. 764) in Mexico examined 93 patients suffering from onchocerciasis; of these, 70 had signs of eye trouble, mostly punctate keratitis, corneal opacities, and iritis. Lesions of the fundus are rare. The keratitis does not interfere much with vision, but the iritis does.

GOLDMAN and ORTIZ (p. 664) describe three types of dermatitis associated with American onchocerciasis.

PEEL and CHARDOME (p. 1159) have found the adult female of *Agamofilaria streptocerca* in *Pan paniscus*.

Enterobius infestation etc.—SCHÜFFNER (p. 233) discusses *Enterobius* infection as he has studied it in Amsterdam, where all the children appear to be infested.

He has found, by experiments in volunteers, that the length of life of the worm is 37–93 days, and that worms are passed 36–53 days after infection. Dust-borne infection is extremely important; the eggs are derived from the skin of the anal region and may be found in rooms, lavatories and, most important, in bed-clothes. In the absence of re-infestation, untreated infections die out in some 12–27 days. For treatment he advises small enemata to clear the lower part of the bowel, and the use of gentian violet; but the question of re-infestation is obviously important. Finger infection can be reduced by washing the hands and the anal region, especially in the morning, so that the day clothes are reasonably free. Close-fitting drawers worn at night may help, but are not the complete answer. The anus may be closed with suppositories or ointments. [It would be interesting to know if the oiling of bed-clothes would be as e ffective in this connexion as it is in relation to pathogenic bacteria.]

HUMMELEN (p. 355) has made a survey of intestinal helminthic infestations in part of Holland; *Ascaris* and *Trichuris* were found, and the incidence was related to poverty and rural life. *Enterobius* was also found, in 72–100 per cent. when the examination was made by the pestle method of Schüffner and Swellengrebel.

KUITUNEN-EKBAUM (p. 940) has used phenothiazine in the treatment of *Enterobius* infection, in 408 children and 176 adults. The first dosage proved too toxic, and most were treated with doses up to 7 gm. total (according to age), administered over a period of 4 days; 80–85 per cent. were negative after the first course of treatment; up to 3·4 per cent. needed three courses. Toxic reactions included anaemia (sometimes needing emergency treatment) and certain minor conditions. The drug should be highly purified, and the patient in good health and not constipated; if toxic reactions occur, it should be discontinued. It is more effective than gentian violet, but more toxic. It is futile to treat one member of a family only, since, as a rule, infection runs through a family.

GETZ (p. 57) produces evidence which indicates that massive infestation with *Trichuris* may give rise to serious illness, which may suggest hookworm disease. The signs include diarrhoea, blood-streaked stools, weakness and loss of weight, pallor, fever, emaciation, anaemia and abdominal distension. He describes the findings in four autopsies carried out on children in Panama, in which very large numbers of *Trichuris* were found along the whole length of the large intestine. There may be no characteristic lesions. WHITTIER *et al.* (p. 577) also state that infestation with *Trichuris* may give rise to severe symptoms, of diarrhoea, bloody stools, pain and tenesmus, with loss of weight. They quote cases seen in the Panama Canal Zone.

Trichiniasis, etc.—The incidence of *Trichinella spiralis* in human autopsies in the United States is 16 per cent., and in hogs 1·5 per cent. GOULD (p. 578) discusses control of this infection, and gives his opinion that it can best be effected by the processing of pork products, by heat, or by freezing at about 0°F. He gives reasons why microscopic inspection of pork may fail, and why the cooking of garbage for hog food may be impossible to enforce. A considerable amount of pork products contain living larvae, and unless these meats are properly cooked, they are dangerous.

NEGHME (p. 577) reports trichiniasis in 12·5 per cent. of bodies from hospitals in Santiago, Chile.

PEPPER and DÍAZ RIVERA (p. 356) give an account of the clinical picture and laboratory diagnosis of trichiniasis, laying stress on demonstration of larvae in the blood. They think that this infection may be more common in tropical countries than is at present realized.

GOULD (p. 362) has devised a new type of trichinoscope.

OLIVER GONZÁLEZ (p. 357) has contributed a long paper on the antigenic differences between the larva and the adult of *T. spiralis*. In infected rabbits, two antibodies are provoked, one against the larva and one against the adult, and these give rise to precipitates about the orifices of larvae and adults respectively, under suitable experimental conditions. The author discusses his findings in relation to problems of immunity to worm infections, but for this discussion the original abstract should be consulted. ROTH (p. 359) has used a serological test for the diagnosis of trichiniasis, in which larvae from infected muscle are placed in the suspected serum. If the patient is infected, precipitates are formed around the orifices of the larvae. Details must be sought in the original, but the author writes favourably of the test.

SUESSENGUTH and KLINE (p. 360) have devised a simple rapid flocculation test for trichiniasis, in which the antigen is an alkaline aqueous extract of *Trichinella* larvae to which cholesterol is added. If this is mixed with serum from an infected person or pig, flocculation occurs which can easily be seen under low power of a microscope. A few results in human trichiniasis are given, and a large number of negative results are recorded in other conditions; the test appears to be fairly specific, but it is possible that false positive reactions may occur. The test can be done in a few minutes, and is likely to be of great value in the testing of swine.

GAASE (p. 236) shows that the complement-fixation reaction may be successfully used in detecting light infections with *Trichinella spiralis* in man.

It had been conjectured that food containing dead larvae of *Trichinella*, killed by freezing or by cooking, could induce a state of allergy in man or animals who consumed that food, and that this might explain the high incidence of positive skin tests in certain communities. AVERA *et al.* (p. 765) have failed to find any experimental evidence in favour of this view. They note, incidentally, that they experienced difficulty with the skin test in guineapigs, and that rabbits and dogs give better results.

DORIN (p. 1057) describes the preparation of an antigen of *T. spiralis* which, after fixation to aluminium cream preparations and injection into rabbits, gives a high degree of active immunity to subsequent infection by larvae. Serum taken from animals thus immunized confers some passive immunity to others infected at about the same time.

PÉREZ ARA and PÉREZ VIGUERAS (p. 580) describe, but cannot identify, a nematode discovered in the lower eyelid of a Cuban patient.

Charles Wilcocks.

MALARIA.

SCHWETZ, J. Sur la limite altimétrique du paludisme en Afrique centrale et ses causes. [**The Limit of Altitude for Malaria in Central Africa and its Causes.**] *Acta Biol. Belgica.* 1942, v. 2, No. 1, 92–5.

The limit of altitude for endemic malaria in Central Africa, as stated by the author, appears to be about 1,750 metres. The absence of malaria above this height is due to the absence of the common Central African anophelines known to transmit the disease, namely, *A. gambiae*, *A. funestus*, *A. marshalli* and others.

Nevertheless, other rare species which are restricted to high altitudes were found at 1,950 and even 2,150 metres. The least uncommon of these were *A. christyi* and *A. kingi*.

[GARNHAM, in this *Bulletin*, 1945, v. 42, 959, reported a severe epidemic of malaria in Londiani, Kenya, in 1941, at an altitude of 7,500–7,800 feet, and

another in 1944 to the north of this area at 8,300–8,500 feet: he also takes into account the mean atmosphere temperature in relation to the limits of anopheline breeding.] *H. J. O'D. Burke-Gaffney.*

i. VAN THIEL, P. H. & WEURMAN, C. L'attraction exercée sur *Anopheles maculipennis atroparvus* par l'acide carbonique dans l'appareil de choix II. [**Attraction of Carbon Dioxide for** *Anopheles maculipennis atroparvus* **in Apparatus II.**] *Acta Tropica.* Basle. 1947, v. 4, No. 1, 1–9.

ii. ——. Attraction exercée sur *Anopheles maculipennis atroparvus* par l'acide carbonique dans un olfactomètre. [**Attraction of Carbon Dioxide for** *Anopheles maculipennis atroparvus* **in an Olfactometer.**] *Ibid.* 10–20, 2 figs.

i. In a previous paper [this *Bulletin*, 1939, v. 36, 1004] the senior author and his colleagues described experiments with a special apparatus in which the feeding preferences of races of *A. maculipennis* were studied.

In the present paper, further experiments were carried out with *A. m. atroparvus* and the authors claim that carbon dioxide, especially if the concentration is 10 to 26 times that of the atmosphere, exercises an attraction on this species, in combination with blood, warmth and moisture, or combinations of some of these factors. Increase of temperature and humidity did not alone exercise the necessary attraction, and the authors therefore assume that the carbon dioxide itself must be regarded as the factor of attraction.

The combined attraction of warmth, defibrinated blood and CO_2 does not, however, reach that degree produced, in other experiments, by the pig.

ii. The use of a modified olfactometer enabled the author to confirm the hypotheses based on experiments with the apparatus previously described; it was demonstrated that *A. m. atroparvus* was attracted by CO_2 up to a concentration of 10 per cent. *H. J. O'D. Burke-Gaffney.*

BURGESS, R. W. **Pigmentation as a Specific Character in certain Anopheline Pupae.** *J. National Malaria Soc.* 1946, Sept., v. 5, No. 3, 189–91, 2 figs.

The author reports that over a period of three years, separation of species of *Anopheles* by pupal colouration has been helpful, so far as laboratory-reared specimens are concerned. He suggests it may be possible to use the method in the field and particularly for separating members of the *A. maculipennis* complex. He briefly notes the character as seen in *A. quadrimaculatus*, *A. maculipennis freeborni*, *A. m. occidentalis*, and *A. punctipennis*. Pupae of *A. crucians crucians*, *A. c. georgianus* and *A. walkeri* are without distinctive markings and must be identified by other characters, unless only one of them is being compared with one of the pigmented species. *H. S. Leeson.*

WHITE, R. Senior. **On the Outdoor Resting of some Species of Oriental Anopheles.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 425–8. [10 refs.]

"1. In three hill districts of East Central India outdoor resting of *Anopheles* is demonstrable in considerable numbers.

"2. Examination of the abdomens of these catches indicates that a dangerously high proportion of *culicifacies* and the *fluviatilis* group are out of doors at a period in the gonotrophic cycle when they are generally accepted as properly being at their feeding site and so susceptible to spray-killing with pyrethrum insecticide.

"3. The anthropophilic indices of certain species, as found at various catching sites, are set out and the possible import of the differences found discussed."

McArthur, J. **The Transmission of Malaria in Borneo.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, May, v. 40, No. 5, 537–58, 1 fig.

Step by step, the author tells the story of his two years' search for an explanation of the peculiar malaria situation in British Borneo [see also this *Bulletin*, 1946, v. 43, 1000]. After much careful and persistent work he was able to prove that *Anopheles leucosphyrus* was the vector and not *A. maculatus*, as had previously been supposed.

He found *A. maculatus* breeding in close proximity to healthy areas, while in highly malarious areas *A. maculatus* was not infected. An experimental area of a square mile was therefore selected and monthly larval surveys were carried out for twenty-four months. During this time, 44,000 larvae were collected and twelve species of *Anopheles* were recognized; they were present in the following percentages: *A. barbirostris* 57, *A. kochi* 17, *A. maculatus* 14, *A. philippinensis* 11, *A. karwari* 1; in this place, larvae of the following species were rare, *A. leucosphyrus*, *A. tessellatus*, *A. aitkeni*, *A. aitkeni bengalensis*, *A. aitkeni palmatus* and a new variety of *A. aitkeni*.

Meanwhile, children were being examined and spleen rates recorded. An analysis of 1,200 records revealed that highest rates were among villagers in the hills; healthy villages were those furthest from the hills, though the latter were situated in areas of most intense anopheline breeding. The hill breeding species were *A. maculatus*, *A. karwari*, the four forms of *A. aitkeni* and *A. leucosphyrus*. The common plain breeders were *A. barbirostris*, *A. kochi* and *A. philippinensis*. Two villages in a ravine were specially studied; one had a spleen rate of 100 per cent. and the other a spleen rate of 25 per cent. The village with the lower spleen rate was surrounded by *A. maculatus* breeding places, some of them up to the doors of the houses.

By means of human bait traps, collections of adult anophelines inside houses were always so small that the author calculated that it would have taken one man with one trap twenty-five years to obtain 500 female *A. maculatus* for dissection. Experiments with animal baits showed that mosquitoes arrived to feed at sundown and disappeared soon after However, when the results of the catches from human and animal baits were compared it was found that seven of the species, including *A. maculatus*, preferred animals to man and that one species only, *A. leucosphyrus*, preferred man to animals in the ratio of 88 to 12. These findings were confirmed by some precipitin tests which showed that all engorged *A. leucosphyrus* contained human blood, while all other species, including *A. maculatus*, contained animal blood.

Thus *A. leucosphyrus* came to be suspected as the vector of malaria. All possible methods of collecting adults and larvae were then employed and payments were offered for specimens of this species. The collectors began to bring in as many as ten to fifteen *A. leucosphyrus* in a morning, taken from defective bed-nets, and the first infected female was found. After 761 dissections had been made, the total of *A. leucosphyrus* found infected was 25 (3·3 per cent.); the other 1,954 dissections of eight other species, including *A. maculatus*, were all negative.

Efforts were then specially directed towards locating the breeding places of *A. leucosphyrus* and they were eventually discovered in the clear spring water at the sources of streams and along the foot-hills. They were tiny seepages with acid reaction (*p*H 6·0 to 6·4) covered with dead leaves, and always under

dense jungle shade, never anywhere else; though other places were breeding other species in plenty.

Adults were found to come into houses on certain nights and not on others; they always came in after midnight, had a feed and departed. Females were found infected in several parts of the island and consequently the author suggests that more dissections are necessary in other parts of the species' distribution.

Finally, there remained the question of control. Several methods were tested and after some failures with paris green and different means of jungle clearing, the method which promised greatest success was being tried out when the Japanese invasion put a stop to the work. The method of choice seemed to be a partial clearing of jungle for a short distance around breeding places (30 feet had been tried) to let in the light and the admission of cattle to the clearings to keep down re-growth; this was done by the creation of grassy lanes following the stream-beds. As a demonstration of actual malaria control the method failed, because it could not be completed, owing to the invasion, but it did succeed in demonstrating an effective method of control of *Anopheles leucosphyrus* which had every prospect of being permanent. It had the advantage too, of being simple, understood by the people and in keeping with their way of life.

[Malariologists and medical entomologists would learn a great deal by reading this fascinating story in the original.] *H. S. Leeson.*

i. COUTINHO, J. O. Distribuição geográfica dos anofelinos do Estado do Rio de Janeiro. [**Geographical Distribution of the Anophelines in the State of Rio de Janeiro.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1946, Sept., v. 11, No. 29, 439–57, 1 map. English summary.

ii. ——. Anofelinos do Estado de Espírito Santo. Distribuição geográfica das espécies encontradas. [**Anophelines of the State of Espirito Santo.**] *Ibid.* 461–72, 1 map. English summary.

i. In the first paper the species of anopheline mosquitoes are listed for twenty-one of the fifty-two municipal areas comprising the State of Rio de Janeiro. *Anopheles darlingi, A. tarsimaculatus* and *A. albitarsis* are recorded as natural vectors of malaria and fifteen other species have been identified.

ii. The second paper lists the species of *Anopheles* for nineteen of the thirty-three municipal areas of the State of Espirito Santo. Eighteen species were identified, of which those named above are the natural vectors of malaria.

H. S. Leeson.

GERDJIKOFF, I. Ueber die Blutbeschaffenheit bei Malaria unter Vitamin C-Belastung. [**The Constitution of the Blood in Malaria in relation to Vitamin C Concentration.**] *Klin. Woch.* 1939, Sept. 9, v. 18, No. 36, 1214–17, 7 charts.

SWYNGEDAUW, J., LE BOURDELLÈS, B. & MASSE, L. Le diagramme électrophorétique du sérum des paludéens. [**Electrophoretic Changes in the Serum in Malaria.**] *C. R. Soc. Biol.* 1947, Mar., v. 141, Nos. 5/6, 290–91. [10 refs.]

LEVICK, C. B. & MACGREGOR, M. E. **Primary Malaria in London Children. Report of Two Cases.** *Brit. Med. J.* 1947, May 31, 764–5.

The first of these cases was in a child of 6, who developed a febrile illness, with pyrexial rises on alternate days: the child was well between the attacks. Quinine was started, despite three negative blood films, when the spleen became palpable after two weeks: the fever ceased at once. Quinine was

continued for ten days, but some days after it was stopped, another rigor occurred and many benign tertian rings were found in a thin blood film. Treatment was on orthodox lines, progress was uneventful, and the patient remained symptom-free, until 7 months after the original attack, when a relapse occurred, which was treated, with apparently complete recovery. The child's father was a Cypriot, but he had been in England for 15 years: the patient had no contact with any relative from overseas: she had lived in Worcestershire, and later, in Welling, Kent, until two months before the malarial attack: during the war there had been a large American military camp near her home.

The second patient was a boy of 2, admitted to hospital with a 3 weeks' history of daily shivering attacks. His spleen was palpable and many benign tertian ring forms were seen in a thin blood film on the day after admission: there was a well-marked anaemia (3 million r.b.c.; 42 per cent. haemoglobin). The child responded well to quinine and was discharged in a month Neither of his parents had been abroad, and there was no history of contact with a malarial case, apart from a grandfather, who had had malaria in 1918, without further relapse. The child had lived in London since he was 2 weeks old, except for brief visits to Bristol and the Isle of Sheppey; in the last named place, the whole family had been severely bitten by mosquitoes in August 1946, a few weeks before the child's symptoms began.

It is pointed out that it is most unlikely that either infection was acquired in London, where the density of population would have led to the recognition of more than one or two cases if infected mosquitoes had been present: no primary case of malaria contracted in London has been recorded for over 25 years.

It is suggested that the children were infected in Welling and the Isle of Sheppey respectively: despite the wide distribution of *A. maculipennis*, indigenous malaria in Britain has been confined almost entirely to the South-East seaboard and the Thames Valley. In 1919, 300 cases were notified; there were 7 in 1945, and five cases are known to have occurred in 1946 [see this *Bulletin*, 1947, v. 44, 169, 278]. *H. J. O'D. Burke-Gaffney.*

NAPIER, L. E. **Primary Malaria in London Children.** [Correspondence.] *Brit. Med. J.* 1947, June 21, 900.

In this letter, Dr. Napier refers to the paper by LEVICK and MACGREGOR [above]. He expresses surprise that no statement was made excluding the commonest form of primary malaria in persons in non-malarious areas, namely, inoculation malaria produced by transfusion from a latent case or from an infected syringe. He suggests that as one of the cases reported showed more than one relapse, it was unlikely to have been trophozoite-induced; yet, negative statements would have been of value. *H. J. O'D. Burke-Gaffney.*

PULLEN, W. **Spontaneous Rupture of the Spleen in Malaria.** *Med. J. Australia.* 1947, Feb. 22, v. 1, No. 8, 241–3, 2 figs.

A warrant officer, aged 31, had been stationed in New Guinea for nine months in 1945: he had never been in hospital with malaria. In October 1945, he returned to Australia and was discharged from the Army in the following month, after 53 months' service. He continued taking 0·1 gm. of suppressive mepacrine daily until January 1946. Late in February he had "attacks of

malaria" every few weeks and treated himself with four or five 0·1 gm. tablets of mepacrine at irregular intervals. This continued until July 15th, 1946: he never felt well during all this time.

In the second week of July, he vomited several times and had vague upper abdominal pain. Before starting work on the morning of 15th he had a sudden severe pain which seemed to "shoot from his right groin to his left shoulder," and he collapsed. The pain later became localized, chiefly in the upper abdomen and left shoulder.

He was admitted to hospital, where benign tertian malaria parasites were found in a routine blood film: the haemoglobin percentage was 63 (Haldane). The patient showed all the features of an acute abdomen: a diagnosis of ruptured malarial spleen was considered but discarded because of the complete absence of any history of trauma; a provisional diagnosis was made of ruptured peptic ulcer, complicated by malaria. An intravenous injection of 10 grains of quinine bihydrochloride was given, and abdominal section performed.

At operation, much fluid blood was seen in the peritoneal cavity: the spleen was about twice its normal size, its capsule was split, and had been stripped from the diaphragmatic surface.

Attempts to mobilize the spleen resulted in free haemorrhage: when this was controlled, the spleen was removed, and the splenic bed drained. The patient's pulse was barely palpable, but throughout the operation he was given a continuous stream of serum, followed by blood; after the operation, further blood was given by drip transfusion. All these steps restored the patient's condition from its very low ebb. The same night, a rigor occurred, which was treated with intravenous quinine and with alkalis. In 36 hours, his haemoglobin was 52 per cent. (Haldane) and on the 21st day, when the patient was allowed up, it was 84 per cent. The patient made a good recovery, and was fully treated for his malaria throughout.

The spleen weighed 18 ounces and measured 15×10×7 cm. Pigment was abundant, but no parasites could be found in stained sections. The spleen is illustrated in two photographs.

In discussing this case, the author points out that whilst malaria in the Services was seen and treated efficiently in its early stages, the return of demobilized ex-Servicemen without medical supervision is likely to be followed by the appearance of malaria in masked and puzzling forms in civilian communities: and doctors should be alert in looking for such complications, particularly in benign tertian malaria, which is apt to be treated lightly, especially by the patient.

The literature of spontaneous rupture of the spleen is discussed, and this includes some Australian cases [but not the recent fatal one described in the *Med. J. Australia* by TORODE (this *Bulletin*, 1947, v. 44, 278)]. Attention is drawn to the fact that such rupture may occur without pronounced abdominal rigidity and in the complete absence of any history of injury. The rapid deterioration in the patient's condition after the peritoneum was opened is also noted.

The author discusses the principle of massive fluid replacement in the seriously injured: in this case, the patient received no less than 4 litres of serum in about 70 minutes, with apparently satisfactory results: it is calculated that his haemoglobin value must have fallen to at least 26 per cent. (Haldane) before an infusion of blood itself became available. This emphasizes that such a patient may survive with a low haemoglobin value, in an emergency of this kind, if the circulating blood-volume is maintained.

The case mortality-rate in rupture of the spleen is discussed, and the seriousness of the condition stressed. *H. J. O'D. Burke-Gaffney.*

HALAWANI, A., BAZ, I. I. & MORCOS, F. **The Antimalarial Chloroquine-Diphosphate (Aralen).** *J. Roy. Egyptian Med. Ass.* 1947, Mar., v. 30, No. 3, 128–36.

Chloroquine (SN 7618) was first synthesized in the United States and its suppressive and curative properties have already been described [this *Bulletin*, 1946, v. 43, 708]. Under the name of Aralen (Chloroquine-diphosphate) the present preparation has been investigated by the authors in Egypt.

Forty-two patients were each given at midday an initial dose of 4 tablets, each containing 0·25 gm., followed by 2 tablets (0·5 gm.) at 8 p.m., at noon next day and at noon on the following day: thus 2·5 gm. were given in 48 hours. All the cases were benign tertian infections, except 6, which were subtertian. Results were controlled by examinations of thick blood films: follow-up was carried out for 3 to 6 months.

Aralen was found to be active against asexual forms of both types of parasite, and against sexual forms of *P. vivax*: in one of two *P. falciparum* infections, in which crescents were present, they persisted for six months.

Patients were rendered afebrile in one to three days, except in two cases in which this result was delayed. Parasites also disappeared in one to three days: the drug was more rapid in action than quinacrine and CAM-AQI [see this *Bulletin*, 1947, v. 44, 698].

Toxic symptoms experienced were vomiting and epistaxis (1 case), headache (4), rigors (1): these were rare of occurrence and brief duration, and left no ill-effects: they were not apparently related to dosage or to the age and weight of the patient. *H. J. O'D. Burke-Gaffney.*

QUEVAUVILLER, A. Un nouveau sel de quinine: le cinchothiénate. [**A New Salt of Quinine: the Cinchothienate.**] *Rev. Paludisme et Méd. Trop.* 1947, May 15, v. 5, No. 36, 97–101, 1 fig. [10 refs.]

SMITH, P. K. **Toxic Reactions following Administration of Atabrine Dihydrochloride.** *J. National Malaria Soc.* 1947, Mar., v. 6, No. 1, 37–40, 2 figs.

Much of the material described in this paper has already been considered in numerous abstracts in this *Bulletin*.

The main interest in the present contribution, which was concerned with the question of flying-efficiency amongst members of the U.S. Air Force, lies in the observation that the incidence of gastro-intestinal activity was high after certain doses of mepacrine hydrochloride. The highest toxicity associated with suppressive doses was encountered when 0·2 gm. or more, as a single dose, was given twice a week on non-consecutive days. Few toxic reactions were found with daily doses of 0·1 gm. [see FINDLAY, above]. *H. J. O'D. Burke-Gaffney.*

BUTLER, M. G. **Atypical Lichen Planus Tropicalis.** *Arch. Dermat. & Syph.* 1947, Apr., v. 55, No. 4, 535–44, 4 figs.

This is a further comprehensive contribution to the study of atypical lichen planus, which has been the subject of several abstracts in this *Bulletin* [see FINDLAY, above, and 1947, v. 44, 499, for further references].

The present author's investigations were based on a study of 247 patients from the Pacific theatre, and seen between October 1944 and September 1945. The number of cases and the details of them presented are unusually large.

There were two deaths, in a white man and woman respectively, and these cases are described in very great detail. One in every twelve patients was a woman, but members of several races were affected.

Despite the history of mepacrine therapy, the author is not convinced that the drug is the true cause of the eruption, although it may have contributed to it: he prefers the explanation that it is caused by some unknown infectious agent limited geographically to New Guinea and surrounding areas.

In a footnote, he adds, however, that since his paper was presented, the summation of opinions describing the disease include evidence of its occurrence in other geographic areas, which increases the probability of mepacrine being considered an aetiological agent.

[The last view will be found in the many references quoted above: nevertheless, despite the appearance of later material than that now presented by the author, his full and interesting study is a valuable contribution to the clinical knowledge of this condition.] *H. J. O'D. Burke-Gaffney.*

BAMI, H. L., IYER, B. H. & GUHA, P. C. **Studies in Antimalarials. Part III. Preparation of Paludrine.** *J. Indian Inst. Sci.* 1946, v. 29A, Pt. 1, 1–8.

SPINKS, A. **Studies on Synthetic Antimalarial Drugs. XVIII. The Absorption, Distribution and Excretion of Paludrine in Experimental Animals.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 30–38, 4 diagrams. [15 refs.]

In making the determinations indicated in the title, Paludrine was estimated by the hydrolytic method of the author previously described [this *Bulletin*, 1946, v. 43, 400; 1947, v. 44, 35]. The dosage administered to rats was 80 mgm. base per kilo by stomach tube and 20 mgm. per kilo when given intravenously. From the concentrations determined in various tissues, it was apparent that the drug was rapidly absorbed. The blood and plasma levels were low and the drug is not retained in tissues to the same extent as mepacrine. After oral dosage, about 5 and 12 per cent. of administered drug was excreted in urine and faeces respectively, but after intravenous dosage the respective figures were 33 and 2 per cent. In the latter case, excretion was mainly into the small intestine, partly in bile, and a much smaller amount appeared in the large intestine. The low recoveries suggest that Paludrine is largely metabolized in the rat. The results obtained in mice were comparable with those in rats. Only small amounts of drug were present in brain and indicate that the blood-brain barrier was not passed. By detailed estimations in the rabbit, it was shown that Paludrine was distributed in a similar way to mepacrine in the tissues but the former attains a much lower concentration in white cells of the blood. The urine was the main channel of excretion and the small recoveries in it and in faeces again indicated that the drug had been to a large extent metabolized by the rabbit also.

J. D. Fulton.

BRODIE, B. B.; UDENFRIEND, S.; BAER, J. E.; DILL, W.; DOWNING, G.; CHENKIN, T.; TAGGART, J. V.; JOSEPHSON, E. S. **The Estimation of Basic Organic Compounds in Biological Material. I. General Principles** [BRODIE, UDENFRIEND & BAER]. *J. Biol. Chem.* 1947, Apr., v. 168, No. 1, 299–309. **II. Estimation of Fluorescent Compounds** [BRODIE, UDENFRIEND, DILL & DOWNING]. *Ibid.* 311–18. **III. Estimation by Conversion to Fluorescent Compounds** [BRODIE, UDENFRIEND, DILL & CHENKIN]. *Ibid.* 319–25, 1 fig. **IV. Estimation by Coupling with Diazonium Salts** [BRODIE, UDENFRIEND & TAGGART]. *Ibid.* 327–34. **V. Estimation by Salt Formation with Methyl Orange** [BRODIE, UDENFRIEND & DILL]. *Ibid.* 335–9. **VI. Estimation by Ultraviolet Spectrophotometry** [JOSEPHSON, UDENFRIEND & BRODIE]. *Ibid.*, 341–4.

In this series of papers a number of simple methods are described for the estimation of organic bases in biological materials. Extraction of the free

bases from tissues is first carried out with the aid of selected solvents, in order to aid separation from metabolic products. Concentration of the extract is then effected in an aqueous medium and determinations of the amount of base present are finally made by fluorimetric or photometric procedures. These methods were elaborated during the late war, in evaluating large numbers of new chemotherapeutic agents for which a knowledge of the tissue distribution of the drugs was essential. Since minute quantities of a substance even less than 1 gamma—may have to be estimated, great care is required in avoiding absorption by glass surfaces ; and in the case of non-polar solvents, the addition of ethanol proved of value. To test the specificity of the methods employed, a comparison of the solubility of the original compound and that of the substance obtained by extraction is made, so that the latter procedure may be modified as required. The fluorimetric method of estimation was found to be the simplest and most sensitive of all, once the best conditions of irradiation, temperature, *p*H of the medium, the use of filters, etc., had been determined. All of these factors can be largely controlled in aqueous medium. When substances are themselves not fluorescent in solution, it may sometimes be possible to confer this property by suitable treatment. Coupling of the base with a diazonium salt to give an azo dye is another useful method of estimation, which is not readily interfered with by substances extracted from tissues. A further method depends on the fact that most salts of methyl orange are relatively insoluble in water but much more soluble in organic solvents. The methyl orange extracted is measured photometrically after transfer to a small volume of acid and the amount of combined base can readily be calculated. This method has proved of particular value in the estimation of cinchonine. Ultra-violet spectrophotometry is the method finally described. Details of all these methods, which can generally be used in the estimation of a fraction of 1 gamma of material, are described for particular substances. Their successful employment, in the forms described above or after adaptation, has been reported by a number of authors.

J. D. Fulton.

WHITE, R. Senior & RAO, V. V. **On the relative Efficiency of Hand and Spray Catching of Mosquitoes.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 411–16.

In studies of the behaviour of *Anopheles* in East Africa, HADDOW [this *Bulletin*, 1942, v. 39, 595] employed the method of hand-catching. RIBBANDS [*ibid.*, 1946, v. 43, 621] criticized this method as failing to capture about 28 per cent. of the actual mosquito population, and in his own investigations preferred to spray with pyrethrum and to make his counts on mosquitoes so killed.

The present authors have not found any reports of comparison of efficacy between the two methods in relation to Indian mosquitoes, and they therefore record the results of searches made at staff quarters along the Bengal-Nagpur railway, by junior inspectors. These consisted of hand catches followed by spraying and counting the mosquitoes captured as a result of each process. The data relate to 26,865 anophelines of 17 species, caught in houses, and the results confirm Ribbands's contention remarkably closely. In cowsheds the proportion caught by hand was much smaller. The results do not permit any deduction on certain other comments made by Ribbands.

The authors conclude that if captures are required for species and sex data only, hand-catching may be omitted ; but if they are for checking treatments with DDT, hand-catching and a search of the floor for dead specimens should be recorded separately, and pyrethrum should not be used. Full tables of results are given.

Charles Wilcocks.

THOMSON, R. C. Muirhead. **Recent Knowledge about Malaria Vectors in West Africa and their Control.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, May, v. 40, No. 5, 511–27. [28 refs.] Discussion 527–36 [BUXTON, P. A.; RIBBANDS, C. R.; SCHARFF, J. W.; WILLIAMSON, K. B.; WALTON, G. A.; HINDLE, E.; MCARTHUR, J.; TREDRE, R. F.; WENYON, C. M.; THOMSON, R. C. M. (in reply)].

Malaria Transmission by Anopheles melas and A. gambiae.—By means of the egg characters and palpal banding described by Muirhead Thomson, it has been possible to differentiate *Anopheles melas* and *A. gambiae*, and thereafter to determine the sporozoite rate of the former. One thousand dissections by the No. 5 Malaria Field Laboratory revealed a 4·2 per cent. sporozoite rate. In the Lagos area, the author was able to arrive at comparative figures of sporozoite rate in *melas* and *gambiae*, exposed to chances of infection as equal as it is possible to find in nature; he concluded that *gambiae* with a mean sporozoite rate of 11·1 per cent. is nearly three times as effective a vector as *melas* with a mean rate of 4·5 per cent. During these investigations, the highest figures for any month were 8 per cent. for *melas* compared with the remarkable figure of 29 per cent. for *gambiae*. The author, therefore, concludes that *gambiae* and *melas* together form a very formidable partnership on the West African Coast.

Breeding Places of Anopheles melas.—The author describes briefly the characteristic breeding places of *Anopheles melas* in the "orchards" of *Avicennia* mangrove of the Freetown estuary.

[A full description of this type of mangrove appears in papers of Muirhead THOMSON and TREDRE: see this *Bulletin*, 1946, v. 43, 93; 1947, v. 44, 488.]

In distinction to conditions in Freetown estuary is the low-lying lagoon area of Lagos; there, the *Avicennia* mangrove is no longer a guiding light to the breeding areas of *melas*. The inter-tidal zone is characterized by great stretches of *Paspalum* grass, and *melas* is found breeding in a wide variety of places in this area. In the Gold Coast, *melas* breeds among the *Paspalum* grass at the edges of small lagoons in which there may be no clear mangrove belt. The author, in the course of his studies over a period of two years, found that even in places where *melas* is enormously abundant it makes use of fresh water only to a negligible extent; therefore, for all practical purposes, *melas* is rigidly confined to the area below high spring-tide mark.

Control of A. melas.—"Bunding" of the breeding-areas appears to be a most effective method for dealing with *melas* breeding, both in the Freetown estuary and around Lagos. At the latter place, GILROY and his staff have carried out this work with thoroughness; it forms a perfect working model for all malariologists who are likely to encounter this problem in any part of the world. [See this *Bulletin*, 1945, v. 42, 786.]

The author refers briefly to the differences in tidal conditions on different parts of the coast, which affect the siting and construction of the bund. He has formed the opinion that bunding may have great possibilities in the Bathurst area of the Gambia Colony. The best method of dealing with *melas* breeding on the Gold Coast has not yet been worked out.

Breeding Places and Control of Anopheles gambiae.—*Anopheles gambiae* remains probably the most dangerous anopheline in the world; in some ways, it proves a remarkably versatile adversary, while in others, it appears to be a narrow specialist with well-defined likes and dislikes, unable to maintain itself unless conditions are exactly suitable. The author refers to his observations on artificial flushing of stream beds in Sierra Leone, a control which had proved very effective against such stream-breeding mosquitoes as *A. minimus* and *A. fluviatilis* in India; after most effective flushing, large numbers of

full-grown *gambiae* larvae and pupae were found in the stream-bed an hour or so after subsidence of the flood. The sunlit pool or puddle usually described as the ideal breeding-place for *A. gambiae* may be negative. This is exemplified on the laterite flats near Freetown, where the proportion of apparently suitable pools for *gambiae* breeding is as low as one in 50; but in the occasional pool, which seemed to satisfy all requirements, whatever they may be, hundreds of larvae and pupae may be taken in a few square feet of water surface.

The author, in his investigations near Lagos, was unable to bring about a substantial reduction either in the number of anopheles or in their infectivity by the regular house-spraying with pyrethrum in kerosene as advocated by EDDEY on the Gold Coast [this *Bulletin*, 1945, v. 42, 255]. Undoubted successes by spray-killing were obtained against *gambiae* in South Africa, and against *culicifacies* in India.

DDT in Malaria Control.—The author refers to the use of DDT as a residual insecticide in houses and to the commonly accepted idea that treatment of the inner walls and ceilings in houses will make them lethal to mosquitoes for two months or possibly longer. In Lagos, he found that, although many *gambiae* and *melas* remain in dark houses after feeding at night, others leave the house at dawn and rest outside. He was able to show that, while a house treated with DDT in kerosene remains free of resting anopheles for weeks afterwards, as early as the 4th day after treatment mosquitoes were entering the hut, feeding on the occupants, and leaving the hut after feeding. Of those escaping in this way, there was no appreciable mortality in the following 48 hours. Within a week of treatment, large numbers of mosquitoes were feeding in the hut every night, all of them leaving afterwards so that nothing was found in the hut on the following day (Muirhead THOMSON, 1947, in the press). Mosquitoes with gland infections were found resting outside the houses in an isolated village which had been thoroughly treated with DDT in kerosene.

The author concludes that, in the Lagos area at least, the dramatic fall in the house catch after treatment with DDT as a residual spray cannot be accepted as definite proof that mosquitoes are being killed.

Anopheline Reduction and Malaria Control.—The author draws attention to the point that our measures to reduce anopheles are usually referred to as anti-malarial, but in West Africa it is not clear at what point the two terms, namely anopheles reduction and malaria control, become synonymous; everything depends on whose malaria we are trying to reduce, that of the non-immune European or that of the indigenous African. He refers to the work of TURNER and WALTON in Freetown during the last 3 years [this *Bulletin*, 1947, v. 44, 640], where the reduction in anopheles density has been great enough to stimulate comparable investigation into the degree of reduction in malaria transmission; to that end, regular blood examination of infants from birth up to 18 months is in process, so that exact data can be obtained regarding the frequency of new infections and their seasonal distribution. The extent to which malaria contributes to the ill-health of adults in West Africa is not known; and before rural malaria control is considered it would appear to be reasonable to find out first exactly how important rural malaria really is in that part of the world.

Discussion.—In the subsequent discussion, Professor BUXTON agreed that, under the conditions of Muirhead Thompson's work, DDT acted more as an irritant than as an insecticide; the mosquitoes within the house were not dying but living, and some were developing sporozoites, which, after all, is the one thing we want them not to do. Perhaps there is a difference in the effect of DDT between the different species of anopheles, and a further and fuller

enquiry will have to be made. Dr. C. R. RIBBANDS thought that heavier applications of residual DDT would be more effective.

On the question of malaria immunity, Dr. J. W. SCHARFF said that experiences in other equally malarious countries, where the difficulties and tragedies entailed in the build-up of solid immunity may have been more closely observed, suggest that a lighthearted acceptance of the burden of malaria, even in rural Africa, may not be wholly justified, when " health " is the final goal.

In the matter of selection of water for breeding purposes by *Anopheles gambiae*, Professor K. B. WILLIAMSON reminded his listeners that Sir Ronald ROSS counselled investigations of the relations of soil and malaria by modern methods; certainly Malayan experience shows that the incidence of malaria is largely determined by soil characteristics. Not much interest has been taken in the subject today.

[In malaria surveys of the Gold Coast mines, it has been noted that *Anopheles gambiae* does not appear to breed in pools which are definitely acid and have a high iron content.]

Dr. G. A. WALTON said it is not very easy to explain why *Anopheles gambiae* chooses to lay eggs in pools recently formed by workmen who have been getting rock out of the ground, and disregards entirely the multitude of adjacent permanent small pools. After quoting other examples, he said the general impression is that some form of human interference definitely excites the female *Anopheles gambiae* to the place where it will lay eggs.

In his reply, Muirhead THOMPSON expressed the view that this whole question of selection of breeding-places required careful investigation in the field.

R. Ford Tredre.

WHITE, R. Senior. **Anopheline Breeding in Ricefields.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 437–68, 1 chart. [Numerous refs.]

The importance of rice-fields as breeding grounds for anopheline vectors of malaria has been the subject of special study, both in past literature and in the field where, with his co-workers, the author has accumulated much evidence which is fully tabulated in this paper. Their importance depends on the species of anopheline transmitting malaria in each locality, and the author concludes that :—

(*a*) when the vector is *Anopheles annularis*, all rice-fields are dangerous ;

(*b*) when the vector is *A. culicifacies* and the transmission period is during the south-west monsoon, fields are dangerous until the rice plant is 12 inches high ; fallow fields are extremely dangerous. After September, breeding diminishes whatever the stage of the rice ;

(*c*) when the vector is one or more of the *A. fluviatilis* group, all non-seepage rice fields are harmless. Seeping rice-fields and fallow are very dangerous so long as the fields are wet ;

(*d*) a great desideratum is a rice experimental station both in a hill area and in an *annularis* plains area, where in addition to strictly agricultural trials, methods of controlling vector-breeding could be studied. *G. Macdonald.*

COVELL, G. **Malaria and Irrigation in India.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 403–10. [16 refs.]

This note, prepared for a meeting of the Central Board of Irrigation, India, amounts to an indictment of the engineer as being responsible for a great deal of malaria by thoughtless construction of irrigation systems ill-adapted to local circumstances ; an example of what should be done by reference to the Tennessee Valley scheme ; and a plea for the inclusion of proposals for anti-malaria work in all engineering projects.

Irrigation by lift, by pipe, by tides and from tanks may be harmful under special conditions. Inundation irrigation, or the use of natural floods, is often a source of danger, but perennial canal irrigation is the most dangerous. The chief sources of danger in practice are in a general raising of subsoil water level, in seepages and leakages from ill-made channels and badly designed crossings, sluices or siphons. The actual canal or the cultivated field are rarely so important as these avoidable by-products.

Illustrative examples include the Irwin Canal Project, the Lower Chenab Canal and the Sukkur Barrage Scheme, all of which had disastrous effects on the health of the population intended to benefit from them. The solution lies in co-operation between the engineer and the malariologist, a solution to which the author has contributed substantially by his constant teaching and by the courses of instruction on malaria for engineers which he has fostered.

G. Macdonald.

VISWANATHAN, D. K. **Experimental Rural Malaria Control Measures in North Kanara District, Bombay Presidency. Part I.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 377–82. [16 refs.]

—— & PARIKH, R. O. **Part II. Preliminary Experiments with DDT.** *Ibid.* 383–91.

In these two papers the authors attempt to assess the relative value of different methods, and combinations of methods, of malaria control in the Kanara District of Bombay Presidency. This is a rural district where malaria is hyperendemic. The carrier is *Anopheles fluviatilis*, which has an average infection rate of 10 per cent., a high anthropophilic index and a considerable tendency to rest out of doors. It breeds in streams, usually with vegetation, and in rice fields.

The standards by which success, or lack of it, was measured were : (*a*) the number of *A. fluviatilis* adults caught in 10 man-hours, 4 being the threshold below which transmission was presumed not to occur ; (*b*) the spleen rate ; (*c*) the parasite rate ; (*d*) the infant parasite rate ; and (*e*) dispensary returns.

The author of the first paper tried the effect of clean weeding of streams alone ; this treatment, combined with copper cyanide treatment of rice fields ; adult mosquito destruction with pyrethrin sprays ; and a combination of all these methods. Naturally, combinations were more effective than single methods, and the complete treatment was speedily effective but too expensive for routine application under rural conditions. The interest to the reader lies in the attempt to analyse the relative efficacy of each method. Although the author gives his own assessment, roundly condemning spray-killing as either ineffective or, if effective, too expensive, the reader is not enabled to arrive at his own conclusion. Data for each set of observations are presented in slightly different forms, which makes comparison almost impossible.

The second paper describes the results of DDT residual anti-adult sprays, applied at the rate of one quart of a 5 per cent. solution in oil per 1,000 sq. ft., in the same area. Again, data are presented in slightly different forms, from which it can be seen that *A. fluviatilis* disappeared entirely from treated houses, and decreased in animal sheds, whilst in untreated villages they are present though without ever reaching the critical level of 4 per 10 man-hours. Spleen and parasite rates were lower in treated than in untreated villages (S.R., 44 and 55 ; P.R., 16 and 21) and there was a significant difference in the infant parasite rate in the two series (2 out of 61, or 3·3 per cent., in the treated series and 10 out of 31, or 32·3 per cent., in the others.)

The cost of the DDT work per head per year was rupee 0–8–0 ; that of the combination of the three methods in the first paper Rs. 0–8–0 ; that of pyrethrum

spray treatment unstated ; that of clean weeding and copper cyanide treatment, Rs. 0–8–0 ; that of clean weeding only, Rs. 0–12–0. The authors conclude that DDT as a control measure is economically feasible, that the combination of the three methods is too expensive for most areas, and that spray killing alone is too expensive for practical use. *G. Macdonald.*

WHITE, R. Senior & GHOSH, A. R. **House Spraying with DDT : Further Results.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 489–508.

The authors continued work previously started by Senior WHITE [this *Bulletin*, 1946, v. 43, 306] on the measurement of the efficacy of DDT residual spray as a malaria control measure. A 5 per cent. solution of DDT in oil was used, the dose being increased, during the experiment, from 1 quart per 1,000 sq. ft. to 1 quart per 600 sq. ft. Reapplications were, for the most part, made when the discovery of sporozoite-infected anophelines suggested that the efficacy of the previous application was decreasing.

The effects on the state of infectivity of anophelines, which are tabulated at length in the original, may be summarized briefly in the following way :—

	A. culicifacies		*A. fluviatilis*		Other anophelines	
	Dissected	Sporozoite rate	Dissected	Sporozoite rate	Dissected	Sporozoite rate
				Per cent.		Per cent.
Control Village	3,041	0	2,032	2·6	539	0·19
Treated Villages	2,021	0	283	0·35	162	0

The reduction in vector density varied from 13·7 : 1 to 227 : 1. There was a greater decrease in *Anopheles fluviatilis* than in *A. culicifacies*, a fact which the authors relate to the normal resting-places of the former species on walls and other places liable to have been sprayed with DDT rather than on furniture and other places likely to escape treatment. There was some reduction in the spleen rates in treated villages ; but as that in the control village also decreased, no deductions can be drawn from this.

There is fairly substantial evidence that the interval between successive applications of DDT may be lengthened, presumably owing to a " reactivation " or re-solution and fresh dispersal of the old deposit. The intervals between successive applications of solution and the finding of infected mosquitoes lengthened in three villages from (1) 75 to 164 days, (2) 57 to 98 days, and

Age of film (days)	Contact (hours)
1–2	1
3–4	2
5	3
6–11	4
13–31	5
31–103	6
110–117	7
120–145	8
152–173	9

(3) 73 to 173 days. The aging of films was tested in the laboratory, and the period of contact with a film of DDT necessary to kill all test mosquitoes was found to increase regularly with the age of the film. With a few minor exceptions, the time of contact needed is as given in above table. *G. Macdonald.*

AITKEN, T. H. G. **A Study of Winter DDT House-Spraying and its Concomitant Effect on Anophelines and Malaria in an Endemic Area.** *J. National Malaria Soc.* 1946, Sept., v. 5, No. 3, 169–87, 2 figs. & 1 map.

Advantage was taken of the presence of extensive flooded areas near the mouth of the Volturno river in Italy to make a full-scale trial of the efficacy of DDT as a residual insecticide. It was applied as a 5 per cent. solution in kerosene and also as a 10 per cent. powder mixed with pyrophyllite. The normal rate of application in 1944 was 60 mgm. per square foot and resulted in effective control for at least 80 days after treatment.

After these preliminary trials, in January 1945, all habitations in a flooded area of about 8 square miles were treated with DDT in kerosene at the rate of 83 mgm. per square foot. A regular record was made of the number of adult and larval mosquitoes in the test area and in a comparable untreated area remote from it. Anopheline larvae were first seen in March, and fresh adults appeared during April. There was a very great reduction in the number of adults in the treated areas, and this continued into the winter season, though no subsequent application of DDT was made. The average anopheline densities per square yard of wall surface (in bedrooms, goat sheds, pigsties and stables) in the treated and untreated areas were :—

	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.
Treated	0·06	0·02	0·00	0·001	0·003	0·05	0·13	0·04	1·06
Untreated	—	—	—	9·87	41·84	167·04	118·5	185·54	185·54

It was noted that adults occurred in relatively great numbers in the vicinity of any untreated shelter, however small, and that spraying of every shelter was necessary for success.

Treatment of the resting-places for adult mosquitoes was accompanied by a great decrease in the numbers of larvae in the neighbouring swamps. The average larval densities per 10 dips in the two areas were :—

	April	May	June	July	Aug.	Sept.
Treated	0·17	0·21	0·32	0·06	0·02	0·00
Untreated	4·00	18·60	11·60	1·00	4·00	—

Spleen and parasite surveys indicated that the reduction in mosquitoes was accompanied by a reduction in malaria. The splenic index, which had been 43 per cent. in 1944, dropped to 25 per cent. in 1945, whilst the parasite index dropped from 21 to 1 per cent. In the control area, malaria remained at its old level or actually increased.

[This work is of particular value in its demonstration of the effect of adult mosquito destruction on the limitation of breeding. The results are much more successful than those previously reported and may be compared with those

achieved by GAHAN and LINDQUIST [this *Bulletin*, 1946, v. 43, 99]. In considering the two sets of results, it should be remembered that artificial flooding of the Volturno area produced unnatural conditions in that all possible resting-places which might have been alternatives to the treated homes were submerged.]

G. Macdonald.

GORDON, I. **The Occupational Hazard of DDT Spraying.** *Brit. J. Indust. Med.* 1946, Oct., v. 3, No. 4, 245–9.

A team of 27 African workers engaged in mixing and applying solutions of DDT in kerosene, often virtually without precautions to prevent skin contaminations, was watched for signs of DDT poisoning throughout the period July to October 1945, though members had been exposed since May. There were no significant changes in weight, in haemoglobin or in blood calcium. [It appears to the reviewer that there may have been significant changes in the leucocyte counts. Of 23 men on whom repeated counts were made, 21 showed an increase, the average increase being of the order of 3,000 per cmm., and the average count of the whole group rose from 6,300 to 8,000. In the absence of further data, including controls, this proves nothing but it suggests the need for closer enquiry.]

Patch tests were mainly negative, and the author concludes that DDT, whilst itself innocuous, enhances the vesicant effect of kerosene.

G. Macdonald.

WATSON, R. B., KIKER, C. C. & HESS, A. D. **A Review of Malaria Studies and Control in the Tennessee Valley in 1945.** *J. National Malaria Soc.* 1946, Sept., v. 5, No. 3, 193–203.

At the beginning of 1945, the stage seemed to be set for an epidemic of malaria in the Tennessee Valley. Immunity was extremely low, the spring was warm and favoured early breeding, and water conditions were unusually suitable for the development of *Anopheles quadrimaculatus*. The non-appearance of the epidemic is attributed partly to the very small number of gametocyte carriers as a result of past control (only 20 out of 15,338 blood films were positive in 1943–4) and partly to continued control, though high mosquito densities did occur.

Control of breeding was on normal lines, that is, management of water level and control of marginal vegetation, supplemented by the use of larvicides, DDT residual spraying and mosquito proofing. Several interesting observations were made of the relationship of anopheline breeding to plants, the methods of removal of plant species proving obnoxious by favouring anopheline breeding. Records are also given of the use of thermal aerosols containing DDT as a larvicide, of their harmlessness to fish, and of the use of DDT as a residual insecticide.

G. Macdonald.

RODHAIN, J. Sur un *Plasmodium* du gibbon *Hylobates lensciscus* Geoff. [**A** *Plasmodium* **in the Gibbon** *Hylobates leuciscus*.] *Acta Biol. Belgica.* 1941, v. 1, No. 1, 118–23, 1 fig.

In June 1939, the author discovered a *Plasmodium* in the blood of a gibbon, *H. lensciscus* [this presumably refers to *H. leuciscus*], which had come from Java.

The parasites were scanty in the blood on 2nd June, more numerous on 7th, and then disappeared.

A very detailed description of the parasite is given and this is supplemented by 7 microphotographs: for the description of the trophozoites, growing forms, schizonts, nucleus and infected red cell, the original paper must be consulted.

A special feature was that of the pigment : in the trophozoites, it was extremely fine, powdery and apparently condensed near the periphery of the protoplasm : as the parasites grew in size, it developed into conglomerations of fine irregular grains, having a peculiar pale brown tinge ; in the female gametocytes, slightly larger and more numerous grains were seen, and these retained their special tint, or rather their lack of deep colour. In dividing schizonts, they collected in one or two masses, having the same distinctive colour.

In discussing the identity of the parasite, the author distinguishes it from *Plasmodium pitheci*, and from the four common species described in the monkeys of Asia, namely *P. semnopitheci*, *P. knowlesi*, *P. cynomolgi* and *P. inui*, on morphological grounds which are described. He considers that it more nearly resembles *P. inui* than it does any of the other forms : but considers that the latter is more amoeboid, possesses more and darker pigment, and is in a slightly enlarged red cell, all of which features distinguish it from the *Plasmodium* found in the gibbon.

These differences, and the fact that attempts to infect the anthropoids (chimpanzee and orang-outang) with *P. inui* were not successful, lead the author to claim provisionally that the blood parasite found by him in *Hylobates lensciscus* is probably a new species, which he proposes to call *Plasmodium hylobati*.

He adds that should new work result in proof that *P. inui* can be transmitted to the gibbon and produce the morphology described, the specific name now proposed would become synonymous with *P. inui*.

H. J. O'D. Burke-Gaffney.

MANWELL, R. D. **Failure of *Aëdes aegypti* and *Culex pipiens* to transmit *Plasmodium vaughani*.** *J. Parasitology.* 1947, Apr., v. 33, No. 2, 167–9.

KYKER, G. C., MCEWEN, Mildred M. & CORNATZER, W. E. **The Formation of Antimalarial Agents by Ultra-violet Decomposition of Quinine.** *Arch. Biochemistry.* 1947, Feb., v. 12, No. 2, 191–9. [15 refs.]

In a previous communication [this *Bulletin*, 1946, v. 43, 706] the authors described the decomposition brought about in certain cinchona alkaloids by ultra-violet light. The present paper deals with the nature of the decomposition as judged by biological and other tests. It was previously reported by ROSKIN that irradiated quinine has a more potent effect on bird malaria than the parent substance (quoted from this *Bulletin*, 1946, v. 43, 300) [GALUSHKINA, *ibid.*, recently made similar claims in the case of human malaria]. The present authors in their tests used Peking ducklings infected with *P. lophurae* by intravenous inoculation of infected blood. Daily intraperitoneal drug treatment was carried out according to body weight of the birds, so that several dosage schedules were represented in each group, one of which received quinine dihydrochloride, while three other groups were treated with irradiated quinine solutions prepared in various ways. A fifth group of birds received no treatment and served as control. The content of each solution was estimated by turbidimetric and fluorimetric methods. One solution which had been extracted with ether was known to contain no quinine. Absolute comparison of quinine and its products of change following irradiation was not possible in the absence of precise knowledge of the chemical and physical properties of the latter. From the results of treatment of infected birds, it was concluded that an antimalarial agent other than quinine was present following irradiation of its solutions.

J. D. Fulton.

GINGRICH, W., SCHOCH, Eugenia W., SCHWAB, Marjorie & SHEPHERD, Catherine C. **Radical Cure of Avian Malaria** (*Plasmodium cathemerium*) **with SN 8557, a Naphthoquinone Derivative.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 147–52, 1 fig. [13 refs.]

In investigating the curative effect of a number of naphthoquinone derivatives in bird malaria, canaries infected with different strains of *P. cathemerium* have been used. Infection was brought about by intravenous inoculation of parasitized blood or through sporozoites, and the resulting infections varied considerably in the mortality caused. The drug SN 8557 and three others were tested by administration of oral doses of 75 mgm. per kilo, in olive oil, twice daily, for periods of 5, 10 or 15 days. Curative effect was investigated in relation to the strain of parasite used, the phase and method of infection, and nature of treatment, for which experimental details are given. In the tests with SN 8557, 61 of 110 canaries were cured, and the best results were obtained in the 15-day treatment. Acute infections in which the exoerythrocytic phase was absent were easiest to cure, and the duration of the latent infections modified the curative rate. Host immunity lasted less than 5 months after cure had been effected. *J. D. Fulton.*

TRYPANOSOMIASIS.

BURTT, E. **Incubation of Tsetse Pupae : the Temperature Range experienced by Pupae kept under Normal Laboratory Conditions at Tinde.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 50–51.

In a previous paper [this *Bulletin*, 1946, v. 43, 827], the author noted better transmissibility and higher infection rates with *G. morsitans* and *T. rhodesiense* when the pupae from which the flies emerged were incubated at 30°C. than at the normal temperature of Tinde laboratory.

These normal laboratory temperatures, and the methods and conditions used in recording them, are now described. A table indicates the maximum and median daily temperatures by months at Tinde laboratory during 1941 to 1945.

This table indicates that the mean daily maximum temperature reckoned in this way sometimes reached or slightly exceeded 30°C. in the period September to December : temperatures over 30°C. were infrequent during the remainder of the year. On the other hand, the median temperature at Tinde laboratory was always below 30°C., by values ranging from some 2°C. during the hottest months to more than 8°C. in the coolest.

The incubation of pupae at approximately 30°C. was therefore not entirely outside the range of normal laboratory conditions, especially in the hot season : there was, however, the difference that while the pupae kept at laboratory temperatures were only exposed to them for a few hours at a time—and to much lower temperatures at night—the incubated pupae experienced the higher temperature continuously. *H. J. O'D. Burke-Gaffney.*

THOMPSON, W. E. F. **Nematodes in Tsetse.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 164.

Nematode worms of the *Mermis* type have been found in tsetse flies by a number of workers.

The present author records finding three specimens of these worms in the dissection of some 1,500 *Glossina morsitans* : the average length was 79 mm. Their chief interest lies in the fact that they seemed to be larger than those

previously recorded and to occupy so much of the abdominal cavity of the tsetse as seriously to incommode it : there was evidence that one fly had been forced to take two meals in an unusually short time, and that it was still hungry when it was caught. *H. J. O'D. Burke-Gaffney.*

VANDERPLANK, F. L. **Experiments with DDT on various Species of Tsetse Flies in the Field and Laboratory.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, May, v. 40, No. 5, 603–20.

The experiments were undertaken to determine if DDT treatments to cattle or to attractive screens could exterminate tsetse fly in a given area. Laboratory tests in which flies were placed on treated hides for short periods were encouraging ; quite brief exposures (5 seconds) were lethal. DDT preparations leaving numerous small crystals were more effective than those leaving fewer larger ones. The larger crystals had a longer persistent effect, however. All species of *Glossina* tested were killed by DDT, but some were more susceptible than others.

Field trials were conducted with treated cattle and treated " trap " screens. Results were estimated by marking flies caught on treated and untreated surfaces and judging the lethality from subsequent recaptures.

It was found that the lethal effect on cattle sprayed with an emulsion (to give about 10 gm. DDT per animal) fell off in about six days ; it was only 100 per cent. for about two days. This rapid loss of insecticidal action was apparently due to herbage brushing off the DDT crystals. It was reduced by using an emulsion containing an adhesive agent which gave persistence for about two weeks. Similar results were obtained with treated screens, but the loss due to rubbing was less. Treated screens (2 m. square with about 5 gm. of 60 per cent. pp′-DDT) were effective for about thirty days. The effect was somewhat reduced during humid or rainy weather. *J. R. Busvine.*

LAWS, S. G. **Trypanosome Counts in *Trypanosoma congolense* Infections.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 116–17, 2 graphs.

Many of the methods employed for estimating the number of trypanosomes present in the circulating blood are unsatisfactory, in that they do not indicate the trypanosome content of a unit volume of blood ; the author refers to a number of methods, based on the use of counting-chambers, standard dilutions of blood and the like [see this *Bulletin*, 1930, v. 27, 237] but has had little success with any of them.

He did, however, obtain consistent results when comparisons were made with the number of leucocytes in a stained thick blood-film, and counts were made on duplicate slides.

Leucocyte counts of oxalated bovine blood, taken from a vein, were made by orthodox methods in a Neubauer chamber : thick smears were made of blood from the collecting-needle and these were stained with 0·1 per cent. aqueous azur II for one or two seconds and then with azur II-eosin for 30 minutes ; this technique stains the trypanosomes well and preserves the morphology of the leucocytes : a stop was placed in the field of the eyepiece, to facilitate counting and to avoid eyestrain.

The ratio of trypanosomes to a fixed number of leucocytes (500 or 1,000) was found, and the number per cmm. calculated from this.

The blood was taken from two Ankole bovines, infected with a pathogenic strain of *T. congolense,* which had been maintained by 42 serial mouse-passages : trypanosome counts were made daily. The counts are shown in two graphs, which indicate the peaks of *T. congolense* in the blood, compared with the pyrexia in the animals.

The author suggests that this work should be repeated on a large scale, in view of the suggestion that there is a rhythmic developmental cycle in *T. congolense* and *T. vivax* infections, and that this may be related to the time at which treatment should be given. It is also hoped that this study may stimulate the production of an accurate, but less tedious technique.

H. J. O'D. Burke-Gaffney.

DAUZIER, Marguerite. Contribution à l'étude de l'immunité contemporaine d'un traitement chimique dans certaines trypanosomoses expérimentales. [**Studies on the Immunity associated with Drug Treatment of certain Experimental Trypanosome Infections.**] [Thesis for Doctorate in Pharmacy.] Université de Paris. Faculté de Pharmacie. Année scolaire 1944–1945. Série Etat, No. 9, 166 pp. [Bibliography.]

The greater part of this thesis covers well-worn ground, without adding much in the way of new phenomena or new interpretations. As is frequent in theses for higher degrees, considerable space is taken up by minutely detailed protocols, which naturally contribute towards an impressive bulkiness, but also, unfortunately, towards mental indigestion in the reader. There might well have been some judicious condensation of these protocols before they were committed to the press. And since the work has been dignified by appearing in print, one would have welcomed more careful proof-reading. Rightly or wrongly, carelessness on the part of the author or publishers in this matter tends to make the reader unduly suspicious of the validity of the work as a whole, and thereby places the author's contribution at an unfair disadvantage. It is disturbing, for example, to find H. Lyndhurst DUKE appearing as LYNDHURST and DUKE, and G. M. FINDLAY as LINDSAY.

The opening chapter is a useful, though not exhaustive, survey of the literature on immunity in trypanosomiasis of man, cattle, and experimental animals. Practically all this material has been abstracted at various times in this *Bulletin* and its fore-runner, the *Sleeping Sickness Bulletin*.

The author's own investigations were conducted with old laboratory strains of *T. brucei*, *T. evansi*, and three varieties of *T. evansi*, *viz. T. marocanum*, *T. annamense*, and a tryparsamide-resistant branch of the last-named strain.

All the animal work was done with rats and mice, though a few rabbits were used to obtain immune serum, for studies on the trypanocidal power of such serum. Immunity was produced, throughout the work, by drug-treatment, the compounds used being Sulpharsphenamine, Tryparsamide, Suramin, Pentamidine, "Anthiomaline", and "Pentastib" (an aromatic pentavalent antimonial).

As has generally been found by others working on these lines, the immunity was always confined to the homologous strain. Its duration was irregular, especially in mice, and rather short-lived, exceptionally extending to as long as a few months in rats immunized against *T. brucei* by treatment with sulpharsphenamine. The usual duration in rats was about twenty days. The author draws attention to the prolonged incubation periods which frequently characterize the infections produced in such immunized animals as are no longer refractory to reinoculation. [FULTON and LOURIE (this *Bulletin*, 1947, v. 44, 403) have recently associated the prolonged incubation periods in such cases with a change in antigenic type on the part of the trypanosome.]

Intravenous inoculations were found to produce infections in immunized mice more readily than intraperitoneal or intracerebral inoculations.

The author believes, on somewhat slender evidence, that the refractory state is to some extent conditioned by the drug used (though not by the size of dose), sulpharsphenamine being regarded as the most successful in producing immunity,

and she writes (p. 160) that "it is undeniable that trivalent or pentavalent arsenic plays a favourable rôle in the formation of antibodies, whilst antimony, which has a rapid ('nette et rapide') action on the trypanosome, does not appear to favour the formation of antibodies". It is not easy to accept this generalization either on theoretical grounds or on the evidence presented.

Baby rats born of immune mothers were found to share the latter's immunity, confined to the homologous strain, for periods not exceeding 20 or 30 days, that is, during the suckling phase. Young rats could also be passively immunized by ingesting (or by being injected with) the serum of an immunized rabbit.

Other sections of the thesis deal with the size of the spleen in relation to body weight (increased when the blood contained parasites, but no greater in immune than in normal rats); the immunity reactions of splenectomized rats (found to be similar to those of unsplenectomized rats, under the author's experimental conditions); and the rectal temperature of rats (found to bear no constant relation to the state of infection).

The author considers that the refractory state exhibited by immunized animals is attributable to a true immunity rather than to a premunition, that is, the immunity is not dependent upon the continued presence of parasites within the host. *E. M. Lourie.*

MERCHANT, D. J. **Streptomycin in Treatment of Experimental Trypanosomiasis in White Mice and Chick Embryos.** *Proc. Soc. Exper. Biol. & Med.* 1947, Apr., v. 64, No. 4, 391–3.

This treatment was not successful.

FRIEDHEIM, E. A. H & VOGEL, H. J. **Trypanocidal and Spirochetocidal Compounds derived from BAL and Organic Arsenicals.** *Proc. Soc. Exper. Biol. & Med.* 1947, Apr., v. 64, No. 4, 418–19.

An account of preliminary observations.

DUBOIS, A. Action du trichlorure d'arsenic sur l'infection expérimentale par *Trypanosoma congolense.* [**Action of Arsenic Trichloride on Experimental Infections by** *T. congolense.*] *Acta Biol. Belgica.* 1942, v. 2, No. 1, 5–10.

The action was definite and rapid in mice, especially by the pulmonary route: the mode of action is uncertain, and is unfortunately related to an extreme toxicity.

RODHAIN, J. Au sujet du développement intracellulaire de *Trypanosoma lewisi* chez *Ornithodorus moubata.* [**The Intracellular Development of** *T. lewisi* **in** *Ornithodorus moubata.*] *Acta Biol. Belgica.* 1942, v. 2, No. 4, 413–15.

VAN DEN BRANDEN, J. F. Réaction de fixation du complément chez des lapins normaux, avec l'antigène à *Trypanosoma equiperdum* et avec l'antigène à *Trypanosoma evansi.* [**Complement Fixation in Normal Rabbits with** *Trypanosoma equiperdum* **and** *Trypanosoma evansi* **Antigens.**] *Acta Biol. Belgica.* 1942, v. 2, No. 1, 26–9.

The blood of normal rabbits did not fix complement in the presence of these antigens.

RODHAIN, J. Sur la spécificité morphologique et biologique de *Trypanosoma pipistrelli* E. Chatton et R. Courrier. [**Morphological and Biological Specificity of** *Trypanosoma pipistrelli* **Chatton and Courrier.**] *Acta Biol. Belgica.* 1942, v. 2, No. 1, 55–8, 1 fig.

RODHAIN, J. Au sujet du développement intracellulaire de *Trypanosoma pipistrelli* (Chatton et Courrier) chez *Ornithodorus moubata.* [**The Intracellular Development of** *T. pipistrelli* **in** *Ornithodorus moubata.*] *Acta Biol. Belgica.* 1942, v. 2, No. 4, 416–20.

RODHAIN, J. & BONE, G. Essais d'infection de la cavité générale de la tique *Ornithodorus moubata* par *Trypanosoma pipistrelli* et *T. vespertilionis.* [**Attempts to infect the General Cavity of** *O. moubata* **with** *T. pipistrelli* **and** *T. vespertilionis.*] *Acta Biol. Belgica.* 1943, v. 3, Nos. 1/2, 5–8.

RODHAIN, J. & HENRY, E. Sur l'existence de *Trypanosoma vespertilionis* Battaglia et *Trypanosoma pipistrelli* Chatton et Courrier chez diverses espèces de Chauves-Souris en Belgique. [**The presence of** *Trypanosoma vespertilionis* **Battaglia and** *T. pipistrelli* **Chatton and Courrier in different Species of Bats in Belgium.**] *Acta Biol. Belgica.* 1942, v. 2, No. 2, 261–4.

RODHAIN, J. Notes sur *Trypanosoma minasense* Chagas. Identité spécifique du trypanosome du Saimiri : *Chrysothrix sciureus.* [**Notes on** *Trypanosoma minasense.* **Specific Identity of the Trypanosome of the Monkey** *Chrysothrix sciureus.*] *Acta Biol. Belgica.* 1941, v. 1, No. 1, 187–93, 2 figs.

HERNÁNDEZ-MORA, Cecilia. Infección natural del *Triatoma capitata* Usinger 1939 por el *Tripanosoma cruzi.* [**Natural Infection of** *Triatoma capitata* **Usinger 1939 by** *Trypanosoma cruzi.*] *Rev. Facul. de Med.* Bogota. 1947, Jan., v. 15, No. 7, 465–80, 4 figs. [30 refs.]

LEISHMANIASIS.

SEN GUPTA, P. C. & CHAKRAVARTY, N. K. **Observations on Agranulocytosis complicating Indian Kala-Azar.** *Indian Med. Gaz.* 1947, Jan., v. 82, No. 1, 11–16, 3 charts.

A full account of three cases ; the usual oral and pharyngeal lesions may be inconspicuous or absent.

SARROUY, C., CABANNES & ROCHE. Trois nouveaux cas de kala-azar du nourrisson et de l'enfant traités par le 2168 R.P. [**Infantile Kala Azar treated with 2168 R.P.**] *Algérie Méd.* 1947, Feb., No. 2, 155, 157–61, 163, 4 figs.

The senior author and his colleagues have already reported favourably on the use of this compound in a single case of infantile kala azar [this *Bulletin*, 1947, v. 44, 55. Six further cases were reported by DURAND *et al.*, *ibid.*, 56]. The present is a detailed account of the results in three other patients.

The cases were all diagnosed by finding L.D. bodies in the spleen. Some of the details may be tabulated as below :—

Case	Age (years)	Weight (kgm.)	Duration of symptoms (months)	Treatment		
				Intramuscular daily for 10 days	Total*	
					as gm. 2168 R.P.	as gm. Antimony
1	1½	9	5	2 cc. first dose, then 3 cc. × 9	8·67	2·465
2	1	6·6	3	2 cc. first dose, then 2·5 cc. × 9	7·35	2·2825
3	8	23·1	1	2·5 cc. first dose then 4 cc. × 9	11·55	3·2725

[* The figures are as given by the authors, but they are clearly not exactly correct, since the proportion 2168 R.P./antimony is not precisely the same in all three cases.]

By about the 4th day of treatment, in all the cases, improvement was obvious, the temperature having settled to normal, the spleen already being smaller and L. D. bodies having disappeared. Improvement continued rapidly, body-weight increasing, and the blood-picture returning to normal. Observation-periods were only 4 months, 1 month and two weeks respectively.

There were no serious toxic effects of treatment, and the authors conclude that this compound is the most efficacious yet known. *E. M. Lourie.*

JERACE, Felice. I flebotomi degli Abruzzi. IVa nota. (*Phlebotomus perfiliewi* Parrot, 1930, trasmettitore della leishmaniosi cutanea negli Abruzzi.) [**The Species of *Phlebotomus* in Abruzzi.**] *Ann. d'Igiene.* 1940, June, v. 50, No. 6, 284–8, 2 figs. [10 refs.]

The author records the presence of and describes *Phlebotomus perfiliewi*, Parrot 1930, in the Abruzzi area : it is the vector of cutaneous leishmaniasis along the coastal zone of central Italy. *H. J. O'D. Burke-Gaffney.*

FEVERS OF THE TYPHUS GROUP.

MORGAN, H. R., STEVENS, D. A. & SNYDER, J. C. **Effect of Streptomycin on Growth of Rickettsiae in Eggs.** *Proc. Soc. Exper. Biol. & Med.* 1947, Mar., v. 64, No. 3, 342–5.

Using a technique described in the paper, the authors found that injections of 2·0 mgm. of streptomycin administered into yolk sacs of embryo chicks two hours before inoculation with *Rickettsia prowazeki* had some inhibiting effect on

the growth of the organisms; with *R. mooseri* a lesser, but still significant, effect was produced, but with *R. orientalis* there was no significant effect.

PABA (*para*-aminobenzoic acid) in doses of 5·5 mgm. caused a striking inhibition of the growth of *R. prowazeki*, and in doses of 11·0 mgm. had a similar effect on *R. mooseri* and *R. orientalis*.

The authors consider it unlikely that streptomycin would have any striking effect on human infection caused by the above rickettsiae.

John W. D. Megaw.

CABASSO, V. **Reaction of the Human Body Louse** (*Pediculus humanus corporis*) **to the Ingestion of Guinea Pig Blood.** *Proc. Soc. Exper. Biol. & Med.* 1947, Apr., v. 64, No. 4, 437–9.

"Contrary to general belief, the experiments reported above indicate that guinea pig blood *per se* is not toxic to the human body louse.

"In the first experiment it was demonstrated that the red blood cells of guinea pigs remain undigested in the gut of the louse.

"In the second experiment it was shown that lice starved for an average period of 36 hours and then fed once on a guineapig, die within 72 hours, apparently of starvation. Control lice fed only on human blood, likewise were found to die 4 to 4½ days following their last human blood meal.

"In the third experiment it was shown that lice fed once on guinea pig blood live their normal life span when their daily feedings are continued subsequently on human blood.

"It would appear that human body lice secrete a digestive enzyme specific only for human red blood cells which makes it impossible for them to digest guinea pig blood."

CABASSO, V. **Mass Infection of Body Lice with** *Rickettsia prowazeki*. *Proc. Soc. Exper. Biol. & Med.* 1947, Apr., v. 64, No. 4, 439–40.

"The experiments reported above indicate that human body lice fed once on a typhus-infected guinea pig at the height of the febrile period, and subsequently fed on a typhus-immune human, develop massive infection with *Rickettsia prowazeki*. In comparison to the rectal inoculation of lice for the preparation of the Weigl type typhus vaccine, this method of infecting lice seems to offer certain advantages."

PACKALÉN, T. **Rickettsial Agglutination and Complement Fixation Studies in Epidemic Typhus Fever.** *Acta. Path. et Microb. Scandinavica.* 1945, v. 22, No. 6, 573–92, 5 figs. [42 refs.]

The author gives a detailed analysis of the results obtained in a large series of serological tests carried out between January 1943 and January 1944, with the object of finding the comparative value of the rickettsia-agglutination (R.A.), complement-fixation (C.F.), and Weil-Felix (W.F.) reactions in the diagnosis of typhus fever.

The author's method of carrying out the R.A. test has already been described by HAMMARSTRÖM [this *Bulletin*, 1947, v. 44, 194]. With this method, the diagnostic titre is said to be 1–20,000 or over; the corresponding titres of the C.F. and W.F. tests were 1–1,200 and 1–200 respectively. Curves showing the rise and fall of the titre in the three tests were in general agreement, except for the great differences in their height.

The C.F. test was regarded as preferable to the R.A. test because of the technical difficulty involved in carrying out the latter test by the author's method. *John W. D. Megaw.*

BARLOVATZ, A. Incubation prolongée de typhus congolais. Auto-observation. [**Prolonged Incubation Period in the Congo Form of Typhus : a Personal Experience of the Author.**] *Ann. Soc. Belge de Méd. Trop.* 1946, Dec. 31, v. 26, No. 4, 323–7.

On December 10th, 1939, in Brussels, Dr. Barlovatz developed an irregular fever, varying from 102° to 104°F. and eventually falling by lysis on the 20th. On the sixth day, a fine macular eruption was seen on the trunk and limbs and a diagnosis of typhus was suspected. There was no albuminuria, the features were, in general, those of the febrile state, there were no complications and convalescence was rapid after a comparatively mild attack. Blood was taken on December 21st for the Weil-Felix test and showed positive *Proteus OX19* agglutinations up to 1/640.

The author adds that 9 days before his illness began, he had visited Dr. Giroud in his laboratory at the Pasteur Institute in Paris, and that the latter later informed him that he had been struck by Dr. Barlovatz's "*tête de typhique*" at the time: had he seen him in North Africa, rather than in Paris, he would have suspected typhus. The author adds, however, that this "*n'est d'ailleurs qu'un détail.*"

Clinically the disease resembled the "Forest typhus" of the Congo previously described by him [this *Bulletin*, 1940, v. 37, 565] and not the more severe "European type". As there was no exanthematic typhus in France or Belgium during this time, the author was perplexed at the origin of his disease, which he considers in great detail.

It appears that in the summer of 1939, he had been in charge of a number of cases of typhus in Maniéma, in the Belgian Congo, and had fed body lice on them in attempts to produce rickettsial infection in the latter. Conditions in the neighbourhood were favourable to infection, and some of the hospital staff did in fact develop typhus.

The author left Maniéma on September 2nd and returned to Europe via Tanganyika and thence by sea to France, calling at Dar es Salaam, Suez and Port Said *en route*: there was no evidence of typhus nor of unhygienic conditions in any of these places. He arrived in Brussels on December 3rd. The incubation period is therefore claimed to have been at least 99 days.

He refers to the occurrence of Brill's disease in the United States, among immigrants from countries where epidemic typhus is endemic, years after their arrival: he also refers to the case recorded in Switzerland in 1946 by MOOSER and LÖFFLER [this *Bulletin*, 1946, v. 43, 543] in an Armenian who had been in that country for 7 years and who had had typhus in Russia in 1918.

The author concludes that his own infection must have been contracted in the Congo and that the incubation period was at least 3 months.

In an ensuing discussion, BRUTSAERT referred to the author's statement that, 9 days before his attack, he had visited a laboratory where typhus research was in progress and suggested that a laboratory infection was possible. The author replied that his visit was a brief one, of about an hour and a quarter, that he was not working there, nor was he exposed to any infected material.

[Nevertheless this last hypothesis cannot be ignored or its possibility excluded completely: it is at least more consistent with the recognized incubation periods than the alternative proposition. Also, in Mooser and Löffler's case, which the author quotes in comparison, the lapse of time between infection and symptoms appears to be related to latency following a known attack,

rather than to an initial incubation period following primary exposure to infection. The fact that the author's attack clinically resembled the milder Congo "Forest typhus" and not the "European typhus, which is generally more serious" is not, of itself, necessarily significant: any form of typhus may be mild.] *H. J. O'D. Burke-Gaffney.*

JUDE, A. & BRUMPT, L. Deux cas de typhus exanthématique survenus après un choc thérapeutique. Discussion sur l'incubation prolongée et la cause déclenchante. [**The Occurrence of Two Cases of Typhus Fever after Therapeutic Shock. Discussion of the Prolonged Incubation Period and the Exciting Cause.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 1/2, 3–8, 2 charts.

The authors briefly describe two cases of typhus fever which occurred in Algiers in early September 1940. Both of the patients were admitted to hospital on the same day; each of them had received an injection of anti-gonococcal vaccine which caused sharp febrile reactions lasting a few hours; the onset of the attack was 12 days in one case, and 10 days in the other, after the therapeutic shock.

The circumstances suggested to the authors that the vaccine may have lighted up latent infections, which probably had been present for considerable periods of time, because no recent source of infection could be detected. It is suggested that latent infections of this kind may play a part in the carry-over of infection from one epidemic to another. An analogy with the prolonged incubation period often observed in malaria is also suggested.

John W. D. Megaw.

SADUSK, J. F., Jr. **Typhus Fever in the United States Army following Immunization. Incidence, Severity of the Disease, Modification of the Clinical Course and Serologic Diagnosis.** *J. Amer. Med. Ass.* 1947, Apr. 19, v. 133, No. 16, 1193–9, 2 charts. [Refs. in footnotes.]

The author states that the excellent results obtained from the use of epidemic-typhus vaccine in the U.S.A. Army are most clearly shown by the fact that, during the period 1942–1945, no death occurred from epidemic typhus among the large number of troops exposed to risk of infection.

Altogether there were 64 cases of the disease, but this low incidence could not be attributed solely, or even chiefly, to immunization, because the troops were thoroughly protected against infection by MYL and DDT powders.

The vaccine used was an ether-treated yolk-sac suspension of the Breinl strain of *Rickettsia prowazeki*. Until the autumn of 1943, the initial vaccination consisted of three doses given subcutaneously at intervals of seven to ten days, and single refreshing doses were given every six months in endemic areas. Later, when improved vaccine became available, only two initial doses were given, and the refreshing doses were given at the beginning and middle of the typhus season.

There was no evidence that the vaccine conferred substantial immunity against murine typhus.

In the official reports of the U.S.A. forces all the louse-borne, flea-borne, and mite-borne typhus fevers are shown together under the heading "typhus fever", but the author assumes (1) that all the cases (603) contracted in the continental United States were murine, (2) that it is reasonable to suppose that the 6,685 cases reported from the south-west Pacific, and China-Burma-India areas, were scrub typhus; and (3) that the 64 cases reported from the European, Mediterranean, and Africa-Middle East areas were of the epidemic type.

[Although this assumption is obviously open to criticism, its adoption does not seriously invalidate the conclusion that the vaccine had a high degree of protective value.]

The paper contains a useful summary of the literature of immunization against typhus fever by vaccines, including 25 references to articles on the subject. *John W. D. Megaw.*

WETZEL, U. Fleckfieberbehandlung mit Rekonvaleszentenblut. [**The Treatment of Typhus with Convalescent Blood.**] *Klin. Woch.* 1944, Aug./Sept., v. 23, Nos. 31/39, 341–2.

BENGTSON, Ida A. **Classification of the Rickettsiae of Rocky Mountain Spotted Fever and of Endemic (Murine) Typhus.** *J. Bacteriology.* 1947, Mar., v. 53, No. 3, 325–7. [15 refs.]

The author describes herself as "retired", but it is to be hoped that this paper will not be the last of her valuable contributions to the literature of the typhus fevers.

The present paper consists of an academic discussion of the nomenclature of the rickettsiae of Rocky Mountain spotted fever and murine typhus.

The former organism is regarded as being more closely related to *Rickettsia prowazeki* than are other organisms which are universally regarded as rickettsiae, so the term *R. rickettsi* Brumpt, 1922, is considered more appropriate than *Dermacentroxenus rickettsi* Wolbach, 1919.

Assuming that the Mexican patients in whose tissues Wolbach and Todd in 1920 detected rickettsiae were suffering from murine typhus, the name *Dermacentroxenus typhi* has priority over the other names proposed for the organisms of murine typhus, such as *Rickettsia manchuriae* (1931) and *R. mooseri* (1932), but as the organism is rickettsial the appropriate name would be *Rickettsia typhi.*

[In the absence of proof that the cases of Mexican typhus were of the murine type, and because the original name is regarded as unsuitable, most workers will probably prefer to use the familiar name *R. mooseri* rather than adopt the inherently inappropriate nomenclature regarded by the author as strictly correct.] *John W. D. Megaw.*

PINTO, M. R. Le typhus murin de l'embryon de poulet. [**Murine Typhus in Embryo Chicks.**] *Arquivos Inst. Bact. Câmara Pestana.* 1945, v. 9, No. 2, 228–42, 2 figs. on 1 pl. [26 refs.]

In a study of *Rickettsia mooseri* the author employed embryo chicks for experiments usually carried out on mammals.

It was found that infection could be transferred from embryo to embryo by the intra-embryonic, intravenous, and intra-amniotic routes. By the intra-embryonic route typical lesions of the disease were produced in the embryo, in which Weil-Felix tests yielded positive results. Immunity tests were also carried out. The intra-amniotic route gave less satisfactory results.

The article is likely to be of interest only to expert workers on the rickettsiae. *John W. D. Megaw.*

ZUIDEMA P. J. "Scrubtyphus" (kliniek en behandeling). [**A Clinical Account of Scrub Typhus.**] *Med. Maandblad.* Bavaria. 1947, May, No. 10, 183–6.

Report of a case and discussion of the literature.

PETERSON, O. L. & FOX, J. P. **The Antirickettsial Effect of Thionine Dyes. I. The Use of Methylene Blue and Toluidine Blue to combat Experimental Tsutsugamushi Disease (Scrub Typhus).** *J. Exper. Med.* 1947, May 1, v. 85, No. 5, 543–58. [27 refs.]

The author carried out a series of experiments on the therapeutic action of various drugs on mice infected with the Karp strain of *Rickettsia orientalis*. The best results were obtained with medicinal methylene blue administered with the food; toluidine blue also proved effective. A high degree of protection resulted when the drugs were given from the time of inoculation, but substantial benefit was observed when the first doses were given after the onset of the illness.

Unfortunately the corresponding scale of dosage of methylene blue could not be tolerated by human beings when given by the mouth, and intravenous administration in adequate doses had been found by other workers to cause haemolytic anaemia.

The striking effect of methylene blue in mice suggested to the author that it might be possible to find a related compound in which the therapeutic element would be dissociated from the toxic element.

Among other lines of study a combination of methylene blue with para-amino-benzoic acid is being tested, and already encouraging results have been obtained.

The paper will be read with great interest by workers on the chemotherapy of rickettsial diseases. *John W. D. Megaw.*

BLANC G. & MARTIN L. A. Non transmission de la Q. fever (virus marocain) par la puce du rat (*Xenopsylla cheopis*). [**Failure of the Rat-Flea to transmit a Morocco Strain of Q Fever.**] *C. R. Soc. Biol.* 1947, Mar., v. 141, Nos. 5/6. 263–4.

YELLOW FEVER.

LAVIER, G. Navigation aérienne et extension de la pathologie exotique. [**Air Travel and the Spread of Tropical Disease.**] *Bull. Acad. Nat. Méd.* 1947, v. 131, Nos. 15/16, 285–7.

A review on the lines of that of FINDLAY, this *Bulletin*, 1947, v. 44, 579.

ANDERSON, C. R. & GAST-GALVIS, Augusta. **Immunity to Yellow-Fever Five Years after Vaccination.** *Amer. J. Hyg.* 1947, May, v. 45, No. 3, 302–4.

The authors discuss the epidemiological evidence regarding the duration of immunity following vaccination with 17D yellow fever virus; and, referring to the findings of BUGHER and GAST-GALVIS, of FOX and CABRAL and of SMITHBURN and MAHAFFY [this *Bulletin*, 1944, v. 41, 478; 1943, v. 40, 451; 1946, v. 43, 34] they suggest that the reports are somewhat conflicting. The first-quoted workers above found that such immunity lasted for 4 years; the second, that it was neither so high nor so lasting in children as in adults; and the third, that the level was as high in children as in adults after 3 years, and that there was no significant change in the proportion of immune persons.

The present authors therefore studied a selected group of vaccinated persons in four Colombian towns in order to assess their immune status since their vaccination about 5 years previously. The towns concerned were Cisneros,

Caracolí, La Palma and Honda, in which no yellow fever had been reported for 20 years: all the persons examined claimed to have resided in their areas all their lives: some of them may possibly have been exposed to yellow fever in the forest.

Sera from the persons selected were usually tested by intraperitoneal injection of mice, but in a few cases where the amount of serum was small, the intracerebral route was employed. Survival ratios of 1 : 6 (or higher values) with an average survival time of 7 days or more were considered evidence of the presence of antibody.

A table shows the results obtained with the 623 sera tested. The percentage showing neutralizing antibodies 5 years after vaccination varied from 91 between the ages of 6 and 9, to 96 in those over the age of 30: the average percentage was 93. Twenty of 65 sera in children of the 6- to 9-year group were from those who were under 3 at the time of vaccination: five years later, the sera of 16 of them (80 per cent.) contained antibodies. Of 45 sera from children who were between 3 and 4 years when vaccinated, 43 (96 per cent.) were positive. Because of the small groups, the authors do not regard this difference as statistically significant, and they conclude that the response of children under 3 does not differ materially from that of older persons.

The authors conclude that, in view of the high proportion of persons of all ages having neutralizing antibodies 5 years after vaccination with the 17D strain of yellow fever virus, revaccination is not required within that period.

H. J. O'D. Burke-Gaffney.

DENGUE AND ALLIED FEVERS.

SABIN, A. B. & BLUMBERG, R. W. **Human Infection with Rift Valley Fever Virus and Immunity Twelve Years after Single Attack.** *Proc. Soc. Exper. Biol. & Med.* 1947, v. 64, No. 4, 385–9, 1 fig.

At least 17 laboratory-acquired infections with Rift Valley fever have been reported. The authors describe a case arising from the "K" strain of virus, obtained from Japan, where it had been incorrectly called dengue. The disease is clinically indistinguishable from influenza and sandfly fever, but has a different effect on mice. Blood from patients suffering from Rift Valley fever kills these animals in 2 or 3 days, whereas influenza and sandfly fever (and dengue) are non-pathogenic to them when inoculated in this way.

The "K" strain of virus had undergone at least 300 intracerebral passages in mice before this infection was acquired. There was, however, no apparent modification in its pathogenicity, possibly because the virus from the first readily multiplies in the mouse and requires no adaptation.

Neutralizing antibodies began to appear on the fourth day after onset and the high titre of 1,585,000 was reached on the tenth day. Antibodies persisted for 12 years after an attack, in the case of another person who was examined.

P. C. C. Garnham.

PLAGUE.

MIYARA, S., CONTE, D., HORENSTEIN, B. & CÓRICA, P. La peste rural en la Provincia de Mendoza. Estudio clinico epidemiologico. [**Rural Plague in Mendoza.**] *Rev. Asoc. Med. Argentina.* 1947, Mar. 15–30, v. 61, Nos. 601/602, 161–82, 17 figs. (3 maps). [24 refs.]

Rural plague in Mendoza, a province of the Argentine Republic, has been sylvatic plague. The authors have collected the data of outbreaks of 1937, '39, '41, '43 and '44, recording a wealth of clinical and epidemiological detail for the several cases. Maps, charts, diagrams and photographs illustrate the article. The epidemic of 1937 differed from the four subsequent outbreaks, which were bubonic and septicaemic, in being pneumonic. The infection in all five years was initiated by sylvatic rodents. The first, 1937, was the most interesting and is illustrated by its nine cases. Two patients presented noteworthy features, one in whom the condition lasted for 11 days, and the other, unique for the Argentine, a recovery from pneumonic plague. As in so many plague outbreaks, recognition of the nature of the first case is not immediate and so it was in the 1937 epidemic. The first patient contracted plague by direct cutaneous infection when he skinned two local wild rodents [*cui*] that he had caught. This is apparently the usual mode of infection in relation to sylvatic plague, where the insect parasites of the rodents concerned play only a problematical rôle as vectors for man. In this respect they contrast with the rat flea of city and port plague. The infected person returned to his home in Mendoza, developed a septicaemic terminal bronchopneumonia and became the disseminator of what developed in due course into primary pneumonic plague. His case had been diagnosed as internal haemorrhage and typhoid, nor was the diagnosis established as plague until the fifth case had occurred. Transmission was interhuman, and buboes were absent. A table of 27 epidemics of pneumonic plague which occurred between 1913 and 1938 shows that 222 individuals died of the 223 involved and that one pneumonic patient survived in the 1937 outbreak.

The next outbreaks are also described in detail; their special investigation revealed that an appalling epizootic of plague of sylvatic type existed throughout the Argentine. This terrible and terrifying drama, as it is called, in the animal population has fortunately not been equalled by anything similar in the human sphere, but the fear remains of communication of plague from the sylvatic rodents to the rats of cities and ports, with the certain production of epidemics of the rat-flea-man type.

Some of the conclusions to this long article are of interest: (1) Pneumonic plague, judging by the freedom from infection of doctors and nurses, requires for its production close proximity to the patient and repeated opportunities for transmission of the disease. (2) Sylvatic plague infection may be comparatively easily avoided if only the rural population is made aware of the danger of handling sick or dead cuis and hares. (3) Sera and vaccines are not regarded by the author as useful prophylactics, nor do the authors regard with any favour quarantine, sanitary cordons of towns and cities, and closure of schools or offices. Nothing surpasses the simple, absolute isolation of patient or suspect in hospital as the best measure of protection for the rest of the population. (4) Deratization is essential for towns and cities, to prevent communication of field rodent epizootics to the rat population, but there is little hope of dealing in the country with the vector fauna of sylvatic plague.

W. F. Harvey.

RAO, S. R. **Rôle of Field Rats in the Endemicity of Plague in H.E.H. the Nizam's Dominions.** *Indian Med. Gaz.* 1947, Feb., v. 82, No. 2, 96–9.

It has long been matter of debate why the rats of plague-ridden Bombay should be highly resistant to experimental infection as compared with the rats of plague-free Madras, which are very susceptible. The same type of problem arises with the question why certain villages within restricted areas suffer from endemic plague while others apparently similar remain constantly free. A direct answer is not given to this question, but an investigation was set on foot to compare the susceptibility of the rats (*Rattus rattus*) of an endemic plague village, Hassegaon, with that of the field rats (*Tatera indica*) around it, by the familiar methods adopted in the Bombay laboratory. It was concluded that "the fact of the field rats in this area being highly susceptible to plague infection, indicates that these have not been in frequent contact with plague infection and as such could not be the cause of endemicity in this area." This negative conclusion, when taken in conjunction with the finding that "rats from the village proper showed a fair amount of resistance to plague infection," has this importance that it would seem a waste of time and money to fumigate rat holes in the fields and that it would be much more profitable to regard the village rat itself as playing the only significant rôle "in keeping this area as an endemic plague zone." *W. F. Harvey.*

PRINCE, F. M. & WAYSON, N. E. **Plague—the Survival of the Infection in Fleas or Hibernating Ground Squirrels.** *Pub. Health Rep.* Wash. 1947, Mar. 28, v. 62, No. 13, 463–7.

Plague is carried over the hibernating period of ground squirrels to become an active disease again, and in the same locality, when the awakening of the rodent takes place in spring. The authors have set up an experiment to determine the mechanism of the process. Six squirrels were used, and 600 fleas in 3 lots: Lot A: 2 normal squirrels, on each of which 100 fleas infected by feeding on infected mice were placed. Lot B: 2 infected hibernating squirrels, each having been inoculated with 0·1 cc. of a plague culture in broth; 100 normal fleas were placed on each squirrel. Lot C: 2 normal squirrels and 100 normal fleas on each squirrel. Artificial arrangements were made for hibernation at 40°F. and at the end of the 4-month period allowed, the squirrels were awake. The results obtained, although not conclusive, are interesting and the experiment is being repeated. In Lot A, neither squirrel became infected, but one of the 14 fleas that remained alive retained *P. pestis* in a virulent form and produced plague when injected into a white mouse. In lot B, one of the two squirrels died of plague; 23 fleas were recovered alive and were plague-free. In lot C, 50 fleas remained alive and were able to reproduce.

Evidently "a flea will remain alive and infected with plague in a virulent form for a period of 4 months in the nest of a hibernating squirrel. . . . Most of the fleas which were infected and remained alive did not retain the infection for the entire 4 months." *W. F. Harvey.*

MEYER, K. F. **The Prevention of Plague in the Light of Newer Knowledge.** Reprinted from *Ann. New York Acad. Sci.* 1947, Apr. 10, v. 48, Art. 6, 429–67, 2 figs. & 2 pls. [69 refs.]

A full half-century survey of the present pandemic of plague, begun in Hong Kong in 1894, brings to us an education and newer knowledge. The defence instituted against the "Black Death" of, (1) sanitation and improved housing, (2) notification, (3) quarantine, did not prevent the continuance of

plague. We can say, however, that plague will never cause the havoc it did 500 years ago. Can this result be explained by the displacement of the domestic rat by the sewer rat, or to the diminution in the prevalence of human parasites? Neither theory is a full explanation of the disappearance of plague from Europe and the Levant, which must be regarded as resulting from intrinsic natural causes.

The foundations of modern antiplague measures were the discovery of the bacillus and, with that, the institution of plague vaccination and serotherapy. Protective inoculation takes a premier place in prevention: yet it is not absolute, for re-infection may take place within a few months, nor have we any accurate information on the immunity enjoyed by persons who have recovered from plague. Controversy is still rife on what form protective inoculation should take—heat-killed broth antigen or agar-grown heat-killed bacilli? Scepticism arose over the significant value of killed bacilli or antigen which, though it is claimed that they reduced the risk of death from plague in British India to one-eighth, they reduced it in Java only by one-half or even only by one-third. This scepticism stimulated a return to trials of 40 years ago, of live avirulent organisms, and produced the "Tjiwidej" vaccine of Java and the "E.V." vaccine of Madagascar.

Such was the position of affairs when at the outbreak of the world war America decided to use formalin-killed agar-grown bacilli in carbolized saline suspension. Experiments on prophylactic immunization were continued and it was found that any plague antigen, or antigenic fraction, stimulated production of antibodies in mice or guineapigs. Confirmation was also forthcoming of the host specificity of immunogenic antigens and demonstration of significant differences in protection as between guineapigs and rats or mice. Protection by any antigen, moreover, was greatly enhanced by synergists such as alum, which double the efficacy. It may be said that these experiments cast considerable doubt upon the reality of the fears expressed as to the efficacy of killed vaccines and upon the claims made for living vaccines: The tests "indicated that it is the actual mass of the bacterial protein rather than the method of preparing the dead antigens that controls the immunisatoric effect. . . . Conclusive evidence has been secured that dead plague antigens with proved immunogenic potency for mice and guineapigs stimulate, in approximately 70 per cent. of human volunteers, the appearance of weak protective antibodies. Further . . . a third injection of 'booster dose' definitely increases the level of the protective bodies." The indications are that the much-criticized prophylactic method of using agar-grown killed antigens would prove effective, if it were used before an outbreak, if inoculations were made repeatedly in dosage of at least 8,000 to 12,000 million bacilli and "provided frequent booster doses were administered."

This review goes on to approve of the usefulness of "rat campaigns in plague-free times which stress systematic building-out of rats supplemented by rodent destruction and the creation of deep rodent-free belts around endangered zones." It commends to special notice the newer rodenticides "Antu" and 1080, while DDT may "revolutionize the suppressive measures against rat-flea-borne plague." "It is not unlikely that domestic rodent plague is again entering a phase of decline . . ., that urban plague, except for a few blighted areas remaining, is no longer a major problem."

Sylvatic plague, as might be expected, receives special emphasis. The saying "no rats no plague" is a slogan which "ignores the fact that wild rodents are potentially more dangerous as endemic foci than are rats." Reference is made to the invasion of the tarabagan districts by Chinese hunters, seeking pelts, in 1910 and to the great epidemic which ensued in Manchuria and claimed 60,000 victims. It was not until 1908 that proof was obtained

in the United States that epizootic mortality among ground squirrels (*Citellus beecheyi*) was due to plague. Investigations "led to the discovery of endemic or epizootic plague among at least 38 wild rodent species in 14 States of the United States." Questions naturally arise as to the potential dangers of sylvatic reservoirs and why in the midst of epizootics, when "the fields and canyons may be littered with carcasses of dead squirrels . . . human cases fail to develop." This is still a mystery. "Until the ecology of sylvatic plague has been thoroughly worked out, isolated observations will continue to serve as a reminder that the existence of plague in the fields and mountains of the Western States harbors as yet unknown potentialities."

W. F. Harvey.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

STEWART, G. T. **The Carrier Rate of Intestinal Infections in Trincomalee.** *J. Roy. Nav. Med. Serv.* 1947, Jan., v. 33, No. 1, 6–8.

The author investigated the stools of 344 Asians and 274 Europeans in Trincomalee.

Examinations were made by means of wet films, concentration methods and cultures on MacConkey and desoxycholate-citrate media.

The Asian group consisted largely of food-handlers from various Service establishments. In 4·1 per cent., trophozoites, and in 9·9 per cent., cysts of *Entamoeba histolytica*, were found. Unidentified cysts were found in 4·6 per cent. and other findings varied from 2·9 per cent. of *Giardia* to 12·5 per cent. of hookworms.

Of the persons harbouring *E. histolytica*, 30 showed evidence of active infection, and therefore 200 apparently healthy Asians were examined, in order to obtain an estimate of the true carrier-rate. This examination revealed the presence of *E. histolytica* cysts in 13 per cent. and of unidentified cysts in 4 per cent. The findings of other parasites were comparable with those in the first group. They were also comparable with the findings of KERSHAW [this *Bulletin*, 1946, v. 43, 557] in respect of the percentage of cysts: but the figures for ova were much lower, probably because of the routine anthelminthic treatment since given to the Asian food-handlers. Finally, in the group of 274 European members of the Combined Services Hospital staff, *E. histolytica* cysts were found in 16 (5·8 per cent.) and unidentified cysts in 4 cases. The only other intestinal parasite encountered was *Giardia*, in 4 cases. Active signs of amoebiasis were found in examination of all of the 16 cyst-passers in this group, although this had not necessitated their reporting sick.

The author points out the significance of the relatively high incidence of active amoebiasis among apparently healthy Europeans and Asians: and taking into account the various factors which frequently limit diagnosis, it may well be that many members of the Services have returned to Europe unaware of their condition and of their infectivity to others.

He also notes the importance of the observed carrier-rate among Asian food-handlers, whose habits might lead to the transference of viable cysts even to cooked food, "so that infected food was probably being served every day in every Service mess in the area."

[The indifference which many residents in the tropics frequently show to "food-sanitation", particularly in communal feeding centres, indicates the need for surveys of this nature to be undertaken widely and persistently.]

H. J. O'D. Burke-Gaffney.

SILVERMAN, D. N. & LESLIE, A. **Intestinal Tumors of Dysenteric Origin.** *J. Amer. Med. Ass.* 1947, Apr. 5, v. 133, No. 14, 994–8, 6 figs. [Refs. in footnotes.]

When intraperitoneal collections of pus undergoing organization are excluded, inflammatory intestinal tumours are almost invariably of a granulomatous nature. In this paper, six cases of tumours of a specific nature are reported as complications of amoebic or bacillary involvement of the intestines. Amoebic granulomata in the colon cannot be distinguished radiologically from cancer. Most cases which have been described, including two of the present series, were subjected to unnecessary laparotomy. As there is such a difference in therapy and prognosis, it is very important to distinguish between amoebic granulomata and malignant tumours.

One case of ileocaecal inflammatory tumour occurred in bacillary dysentery and one in a mixed infection of amoebic and bacillary. The first case of amoebic granuloma was detected in a white man of 19, in whom a filling defect was detected involving the caecum and ascending colon; special barium examinations revealed a constant irregular narrowing of the terminal 5 cm. of the ileum. Faeces culture revealed an organism of the *Sh. flexneri* group. One-stage resection of the tumour was performed with anastomosis of the ileum to the transverse colon.

In another somewhat similar case, *Sh. shigae* was isolated from the faeces, whilst the tumour, on surgical removal, proved to be amoebic. Unfortunately, the patient died and at autopsy the obstructing mass proved to be an amoeboma and there were multiple abscesses of the liver.

The authors question why sometimes amoebic infection of the colon takes the form of extensive ulcero-necrotic process, as in three fatal cases they recently described [this *Bulletin*, 1946, v. 43, 39] (in two complicated by concomitant infection with a dysenteric organism), whilst in others there is a granulomatous response.

Probably this is due to competition between the destructive activity of the amoeba and the regenerative power of the host. When the infection is sudden, there is no time for marshalling the defences against invasion.

The outstanding and almost universal characteristic of amoebic granulomata is their response to specific therapy; and the rapid resolution of large tumours after the administration of emetine hydrochloride is only paralleled by the melting away of syphilitic granulomata after exhibition of iodides. [There are reasons for believing that this statement is not invariably correct.] Rectal scrapings, or even biopsy if a tumour is within reach of the sigmoidoscope, can be diagnostic—careful examination of a saline-purge stool will usually, in most instances of amoebic tumour, reveal *E. histolytica*, but in isolated instances, when these organisms are present only in the depths of the tumour mass, it may not be possible to demonstrate them, so that it is necessary to resort to specific therapy as a means of diagnosis. *P. Manson-Bahr.*

ANDERSON, H. H., JOHNSTONE, H. G. & HANSEN, E. L. **Experimental Chemotherapy of Amebiasis.** *Amer. J. Trop. Med.* 1947, Mar., v. 27 No. 2, 153–60. [13 refs.]

While recognizing the value and limitations of emetine in amoebiasis, the authors have sought new and more effective agents for this disease. Drugs were first screened by an *in vitro* technique in which *E. histolytica* cultures grown with a single organism were exposed to the action of drugs at 37°C. for a period of 48 hours. To avoid the use of solid media which deviate drugs to a considerable extent, a liquid liver medium and a newly devised synthetic

liquid medium [not described] were employed. Some attention was also paid to the mechanism of drug action. By such methods, the action of more than 200 chemical agents, including that of subtilin on the parasite, was studied. A few of these drugs proved more active than emetine in the test tube. [Some of the authors' results, however, apply to experiments in which solid medium was used.] As a guide to drug toxicity for host cells, the effect produced on the mobility of rabbit white cells was studied. In conjunction with the *in vitro* tests, treatment of monkeys infected with *E. histolytica* was carried out for periods of 5 to 30 days with the most promising substances. Generally examinations of a single faecal specimen were made over a period of six consecutive days. Examinations were similarly made from the day after completion of treatment, and again 6 and 12 weeks later, before a monkey was regarded as cured. Tests of liver and renal function and electrocardiograms were made during treatment. Carbarsone oxide proved an active substance in monkey infections, as did two other trivalent arsenicals (thioarsenites), and the first was also effective in clinical trials in man. The authors consider that there is a definite correlation between the results obtained *in vitro* and in monkeys and it is hoped that it will hold in the case of man. A short summary is given of the possible mechanisms by which drugs exert their amoebicidal effects. *J. D. Fulton.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Moreno Berdugo, J. & Infante Gómez, A. Notas sobre una epidemia de fiebre recurrente en Villa Nador y su territorio. [**Notes on an Outbreak of Relapsing Fever in Villa Nador and its Environs.**] *Med. Colonial.* Madrid. 1945, Nov.–Dec., v. 6, Nos. 5/6, 336–63, 11 figs. [25 refs.]

This outbreak, which occurred in March–July 1945, comprised 168 cases under the authors' observation, 108 in the Villa Nador district and 60 in Driuch. The spirochaete present was not determined ; *Sp. hispanica* would be expected, but *Ornithodorus* was not found ; lice, however, were abundant. Infection spread rapidly ; among the army there had been 209 cases up to the end of August. It is thought that infection was primarily introduced by persons coming from French Morocco.

Clinically, the usual incubation period was 6 days, and the symptoms were typical. The first febrile period varied from four days to as many as eleven in three cases, and 12, 14 and 15 respectively in three others. Many of the patients showed a high pre-critical rise of temperature (well shown in some of the charts) ; the afebrile period was 5–8 days and the first relapse 2–5 days. About one-fourth of the patients showed a petechial rash and 4·7 per cent. a labial herpes. Splenomegaly was not marked and practically all with this sign had more or less recently suffered from malaria. Of complications a tendency to haemorrhage was noteworthy, profuse epistaxis, menorrhagia, haemoptysis (rarely) and, in one patient, haematuria. Red corpuscles were reduced to about 2½ million (the lowest was 1,960,000) per cmm. ; most patients had a mild leucocytosis up to 13,000, but 11·8 per cent. showed a degree of leucopenia with reduction even to absence of eosinophiles. There was only one fatal case. *H. Harold Scott.*

PINTO, M. R. Caractéristiques d'une souche de *Borrelia recurrentis* isolée au Portugal. [**Characteristics of a Strain of** *Spirochaeta recurrentis* **isolated in Portugal.**] *Arquivos Inst. Bact. Câmara Pestana.* 1945, v. 9, No. 2, 224–7.

The author gives the characteristics of a spirochaete isolated from a patient who worked as a weeder and mower on a farm near Lisbon, described by FONSECA, LACERDA and PINTO in 1942 and 1943 [*Medicina Contemporanea*, 1942, v. 60, 299, & 1943, v. 61, 78.] The strain resembles *Spirochaeta hispanica* in its general characters including pathogenicity to laboratory animals. Cross-immunity tests were made with a strain from Madrid, and animals immune against the Lisbon strain were susceptible to the Spanish strain, and conversely those immune against the latter could be infected with the Lisbon strain. *E. Hindle.*

CULWICK, A. T. & FAIRBAIRN, H. **Polymorphism in** *Treponema recurrentis* **and** *Spirochaeta vincenti.* *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 1–5, 4 figs.

The electric charge of stained specimens of *Spirochaeta recurrentis* was determined on thin blood films in the manner described for trypanosomes [this *Bulletin*, 1947, v. 44, 649], and the lengths of 774 of these two electrical variants were measured. The length distributions were analysed, and were found in each case to consist apparently of three populations with lengths distributed normally about the means. The sum of the frequencies of the calculated curves fitted closely to the observed values. *S. recurrentis* is thus assumed to consist of six types of individual—short, intermediate and long forms, each of which may bear either a positive or a negative electric charge.

Trypanosoma rhodesiense was found by the authors (*loc. cit.*) to contain the same six forms, and they suggested that these types were maintained by a process of syngamy. The suggestion is now put forward that the occurrence of such forms in *S. recurrentis* may be evidence that this organism also undergoes syngamy.

The lengths of 778 *Spirochaeta vincenti* from a throat swab were next examined, and in this case a series of three normal curves was found to give a good fit to the observed measurements. The electric charge could not be determined, so no decision could be reached as to whether each of the short, intermediate and long forms was composed of a single type or was an admixture of positively and negatively charged variants with mean lengths close together. *J. C. Broom.*

i. WITTEBOLLE, P. Tentatives de culture et d'infection au moyen d'un à plusieurs éléments filamenteux ou granulaires de *Borrelia duttoni.* [**Attempts at Culture and Infection by means of one or several Filamentous or Granular Forms of** *Spirochaeta duttoni.*] *Acta Biol. Belgica.* 1943, v. 3, Nos. 3/4, 190–91.

ii. —— & BAERT, H. Obtention de sous-cultures au moyen d'un seul élément filamenteux ou granulaire de *Spirillum bruynoghei.* [**The Production of Subcultures by means of Single Filamentous or Granular Forms of** *Spirillum bruynoghei.*] *Ibid.* 188–9.

i. The first paper comprises the results of attempts to produce cultures and also to infect mice from tissues of *Ornithodorus moubata* infected with *S. duttoni.* These tissues never showed filamentous [=spirochaetal] forms, but only granules. All attempts to obtain cultures from them were unsuccessful, but subcutaneous inoculation of 0·1 cc. of an emulsion of the tissues into mice produced infection with spirochaetosis.

It required at least 100 filamentous forms isolated from the blood of an infected mouse to transmit the infection, but no reaction followed the inoculation of a similar number of culture spirochaetes.

ii. The second paper contains a description of the isolation of single filamentous or granular forms of *Spirillum bruynoghei* by the use of the pneumatic micro-manipulator invented by Fonbrune. Out of 32 attempts, the authors succeeded four times in obtaining cultures of spirilla by the inoculation of a single granule only 0·2μ in diameter. They also succeeded in obtaining cultures by the inoculation of single spirillar forms. They consider that their technique excludes the possibility of an invisible stage of the organism. They are also of the opinion that their results prove that the granules, not only of spirochaetes but also of spirilla, are not degenerative forms, but a stage in the development of the filamentous spiral form. *E. Hindle.*

SCHWETZ, J. Sur plusieurs foyers de spirochétose du Congo oriental. [**Several Foci of Spirochaetosis in the Eastern Congo.**] *Acta Biol. Belgica.* 1942. v. 2, No. 3, 326–9.

Ornithodorus moubata is common, but unevenly distributed, in the eastern part of the Belgian Congo, especially on the banks of the Great African Lakes. Nevertheless, relapsing fever is not common and the parasite is rarely seen in the blood of local Africans, who have possibly become immunized to it.

The author set himself the task of investigating the degree of infectivity of these ticks.

The ticks were found in five foci on the eastern border of the Congo, namely, Nyangezi, Nzulu, Kisenyi, Gety and Bogoro. No cases of relapsing fever were found and blood examination of 485 inhabitants was negative.

Attempts to transmit the spirochaetes to rats were only successful when large numbers of fully-developed adult ticks were used: when a few adults, and more especially nymphs, were used, the experiments were almost entirely negative. Only a certain proportion of the *O. moubata* in these foci were thus found to be naturally infected. *H. J. O'D. Burke-Gaffney.*

BRUYNOGHE, G. & RONSE, M. Spirille pathogène. [**A Spirillum Pathogenic to Man.**] *Acta Biol. Belgica.* 1942, v. 2, No. 2, 187–9.

The authors isolated a spiral organism in pure culture, from the blood of a febrile patient, after 9 days' incubation in blood-broth.

Young cultures consisted of short forms, having 1 or 2 spirals and showing rapid movement comparable to *Spirillum minus*, but they were short enough to be confused with vibrios. In older cultures, longer forms were seen, containing from 13 to 15 spirals (average 6 to 8) and showing a slower, corkscrew movement, like spirochaetes. The organisms stained easily, and were Gram-negative: prolonged staining with fuchsin by Cazares-Gil's method, showed the presence of fine but definite flagella, usually at each end, but in one case in a tuft of 4 or 5 at one extremity.

The organism was easily cultivated in broth enriched with blood: in ordinary broth, aerobic culture was not satisfactory but, anaerobically, abundant serial cultures were obtained, especially when 0·1 cc. of 0·1 per cent. ascorbic acid was added to the medium.

After several passages in blood agar, anaerobic and aerobic growth developed on plain agar: the forms thus obtained were all short, but typical forms were obtained on subculture in blood-broth.

The authors hesitated in classifying this spiral organism either as a spirochaete or a spirillum: they therefore examined its behaviour in bile and saponin; no lysis occurred in either.

The organisms proved to be non-pathogenic to rabbits, guineapigs, white mice and rats, the first named having been injected intravenously, and the others intraperitoneally.

The patients' serum, taken 12 days after "septicaemic symptoms" agglutinated the organisms in a dilution of 1/3,200: they were lysed at 1/400. Two months later, agglutination took place at 1/400 to 1/800, but no lysis occurred.

The authors note that, apart from *S. minus* "which is not cultivatable" [this statement is open to doubt], they are unaware of similar organisms having been described as pathogenic. They consider that this organism resembles in many respects the organisms described by PONS as *Spirochaeta sinensis* [this *Bulletin*, 1924, v. 21, 471] and by TROISIER [*ibid.*, 1937, v. 34, 708] as *Spirochaeta haemophilus*, but it is distinguishable from these by the fine flagella and certain minor metabolic differences, which are being studied and which will be made the subject of a further report.

H. J. O'D. Burke-Gaffney.

LEPROSY.

AMARO FERNÁNDEZ, J. M. Contribución al estudio de la lepra en Marruecos. El subfoco Jaldi. [**Leprosy in Morocco. A Sub-focus in Jaldi.**] *Med. Colonial.* Madrid. 1946, Aug. 1, v. 8, No. 2, 127–45, 4 figs. [22 refs.]

In the Gomara area of Spanish Morocco, leprosy is known to be endemic; just to the north of this lies Jaldi, and the author has found that the disease is present there also. The inhabitants are pastoral and agricultural. Ten cases are considered in this paper, one female and nine males; as for age, one was in each of the second, third and fourth decades, three in the fifth, two in the sixth, and two were over that age. Various degrees and types were seen; three are classed as L_1N_2, two as L_2N_1 and one each as L_1N_1, L_3N_1, L_2N_2, L_1N_3 and L_3N_3. Six have died, three after less than three years' illness and three others before the tenth year of their disease. *H. Harold Scott.*

IGNACIO CHALA H., J. & LLERAS RESTREPO, F. Ensayos con leprominas filtrada y bacilar desintegrada. (Reacción precoz.) (Nota preliminar.) [**Tests with Lepromin Preparations.**] *Rev. Facul. de Med.* Bogota. 1947, Jan., v. 15, No. 7, 442–64, 2 figs. & 4 charts. [70 refs.] English summary.

After preliminary remarks on the Mitsuda lepromin reaction, the authors describe three lepromin preparations used by them in these tests. They emphasize that the intradermal lepromin test is *not* a diagnostic measure, but is useful in classifying the type of disease, and in determining its severity, evolution and prognosis.

In the present series of experiments three preparations were used: Whole lepromin, filtered lepromin, and bacillary disintegrate lepromin.

1. *Whole lepromin* (lepromina integral) prepared from lepromata rich in bacilli, in patients who had had no treatment. The tissue is boiled in physiological saline for one hour, then cut into small pieces, dried *in vacuo* and ground to powder in a mortar. Saline is then added in proportion of 10 cc. to 0·4 cgm. of the powder and the mixture again ground up, allowed to settle and the

supernatant fluid decanted ; this process is repeated " several times". To the final product 0·5 cgm. phenol (or merthiolate) is added to every 100 cc. and put up in ampoules of 1–5 cc. and sterilized at 120°C. for 45 minutes.

2. *Filtered lepromin.*—The leproma after being boiled and cut up is triturated to a paste and filtered and the filtrate concentrated to one-tenth at 58°C., so that 1 cc. equals 1 gramme of the leproma. It is then put up in ampoules and sterilized.

3. *Bacillary lepromin.*—The leproma is triturated and chloroform added (25 cc. to each gramme of tissue) ; the chloroform is separated, the whole evaporated in a waterbath, the residue is suspended in ether, centrifuged to throw down the bacteria ; the ether is decanted, the process repeated and the deposit (extracted bacilli) triturated and suspended in phenol saline and sterilized after putting in ampoules as before.

With each, 0·1 cc. is injected intradermally into the scapular area. The early reaction is noted after 48 hours and is regarded as positive if there is an erythema more than 4 mm. in diameter with an infiltrated centre. The late, or delayed, reaction is noted in four weeks and in a strongly positive case presents a papule or nodule of 5 mm. or more, perhaps with central necrosis or ulceration.

The results in different types of leprosy are noted, and the author makes the following conclusions :—

1. The early reaction to " filtrate " and " bacillary disintegrate " antigens has the same significance as the Mitsuda reaction, whether positive or negative, and without the undesirable effects of the latter test : the early reaction with whole lepromin sometimes had the same value as the Mitsuda.

2. The disintegrate antigen is more active, and produces more intensive early reactions than the filtrate.

3. The early reaction with filtrate and bacillary antigens is of practical importance in clinical selection of cases.

4. Strongly positive results are obtained with early reactions to both of these antigens and with late reactions to whole lepromin in typical tuberculoid leprosy : simple macular or anaesthetic neural types give negative or slightly positive results.

5. Focal reactions in cutaneous lesions were sometimes met in tuberculoid cases, especially with the bacillary antigen.

6. The use of bacillary disintegrate antigen is recommended for routine work.

Percentages are given in support of the results, and the reactions are also illustrated by photographs : but the totals on which the percentage figures are calculated are not given. *H. Harold Scott.*

MUIR, E. **The Sulphone Treatment of Leprosy.** *Brit. Med. J.* 1947, June 7, 798–801.

BRITISH MED. J. 1947, June 7, 813–14. **Leprosy and its Problems.**

This paper deals mainly with reports on trials of these drugs by American workers at Carville and by Muir in Trinidad, which have already been reviewed in this *Bulletin* [see 1946, v. 43, 458 ; 1947, v. 44, 326–327]. The drugs are of special value in advanced lepromatous cases in which chaulmoogra preparations commonly fail, and for eye complications, which have hitherto usually gone on to produce total blindness, but whose progress can be stopped and some improvement be effected by the intravenous use of promin or oral administration of diasone. They appear to act through preventing the production of new lesions by the dissemination of lepra bacilli through the blood stream, often accompanied by fever, and the gradual death of the organisms in the old lesions. In advanced

lepromatous cases, the treatment has to be continued for four or five years, but FAGET has now reported 19 cases treated with promin which have been bacteriologically negative for 1–2½ years without any relapses; diasone treatment has not yet been used for such long periods, but appears to be equally effective so far. Muir now reports that a few early war-time lepromatous infections have been cleared up within four to six months. The drugs at present cost £6 per case per year. The patients must be carefully watched for the occurrence of anaemia, which requires temporary cessation of the drugs and the giving of iron and liver treatment. Others of this series of drugs are now available for trial, so it is hoped that even more effective ones will be discovered and that with increasing demand they may become available at lower prices. The early discovery of cases, through regular examinations of all known contacts with infective patients, will continue to be necessary to allow of early and more economical treatment. This would tend to prevent the development of the most highly infective stages of cutaneous cases, and lead to eventual disappearance of the main sources of infection and the rapid reduction of the incidence of leprosy during the next few decades.

L. Rogers.

HELMINTHIASIS.

MEIRA, J. A. Tratamento das verminoses. [**Treatment of Helminthiasis.**] Reprinted from *Rev. Gazeta Clinica.* 1946, May–June, v. 44, Nos. 5/6, 93–121.

A review of current therapy.

SCHWETZ, J. & DARTEVELLE, E. Sur les mollusques trouvés dans plusieurs foyers de bilharziose intestinale de la bordure orientale du Congo belge. [**Snails found in certain Foci of Intestinal Schistosomiasis on the Eastern Border of the Belgian Congo.**] *Acta Biol. Belgica.* 1942, v. 2, No. 1, 51–4.

In Bobandana the authors found *Planorbis choanomphalus*, *P. stanleyi* and snails of other genera; in Irumu *P. adowensis* and *Physopsis africana*; in Mongbwalu *P. adowensis*. At Kasenyi on Lake Albert the position is complex, and here the schistosomiasis infection rate in the population is from 25 to 40 per cent. *P. boissyi tanganikus*, *P. choanomphalus*, *P. stanleyi* and *P. adowensis*, all known intermediate hosts of *S. mansoni*, are found in a river flowing into the lake. It had formerly been thought that infestation here was closely correlated with the fishing industry in the lake, but it now seems more likely that infection is contracted by villagers when they bathe in the river, rather than while fishing in the lake.

Two genera of small snails, *Gyraulus* and *Segmentina*, are also found, but their rôle in transmission is not known. *Charles Wilcocks.*

SCHWETZ, J. & DARTEVELLE, E. Sur l'écologie de quelques Planorbes du Congo oriental. [**The Ecology of several Species of *Planorbis* in the Eastern Part of the Belgian Congo.**] *Acta Biol. Belgica.* 1943, v. 3, Nos. 3/4, 298–301.

The authors have examined collections of species of *Planorbis* found in the Belgian Congo; they give the following information about them:—

P. salinarum Morelet has been found in foci of *S. mansoni* infection in Bas-Congo; it also occurs in Western Congo and Katanga. *P. katangae* Haas is found in the south. These two species live in rivers, streams and ponds.

P. tanganikus Bourguignat [? *P. boissyi tanganikus*, see preceding abstract]

(and the related *P. sudanicus* v. Martens), *P. smithi* Preston, *P. choanomphalus* v. Martens, *P. stanleyi* E. A. Smith (*P. bridouxi* Bourguignat) and *P. adowensis* Bourguignat are confined to the eastern part of the Congo. *P. adowensis* is a riverine species; *P. smithi* and *P. choanomphalus* are lake species; *P. tanganikus* is probably chiefly a lake species; *P. stanleyi* is eclectic—it inhabits lakes, ponds and streams.

Two small planorbids, *Gyraulus* and *Segmentina*, are found in Bas-Congo and in the marshes and streams about Lake Albert, as well as in the lake itself.

Charles Wilcocks.

PONCE PINEDO, A. M. **Schistosomiasis Mansoni in the Republic of Santo Domingo. With a Report of Six Cases studied.** *Puerto Rico J. Pub. Health & Trop. Med.* 1947, Mar., v. 22, No. 3, 308–15. [Refs. in footnotes.] [Spanish version 316–24.]

The author shows that early reports of *S. mansoni* infestations discovered in the Republic of Santo Domingo cannot be regarded as evidence of autochthonous infection, since there was no proof that the patients had not been infected elsewhere. He describes the first autochthonous case, diagnosed in 1942, and five other cases seen by him. These patients, and some others, all lived in the Hato Mayor area of the Dominican Republic, and in a small creek in that area the author found innumerable *Australorbis glabratus*, of which some 5 per cent. were infected with fork-tailed cercariae. From these snails, rabbits were successfully infected, and adult *S. mansoni* were recovered from them.

Charles Wilcocks.

PRATT, Caroline K. & OLIVER GONZÁLEZ, J. **Intradermal Reactions to Fresh and Stored Antigens prepared from Cercariae of** *Schistosoma mansoni.* *Puerto Rico J. Pub. Health & Trop. Med.* 1947, Mar., v. 22, No. 3, 254–6. [Spanish version 257–9.]

The authors compared the potency of antigens prepared from *S. mansoni* cercariae, when these were used fresh and after storage at 6°C. for 3, 6, 9 and 12 months.

The dry cercariae powder, from which the antigen was prepared, had been made from cercariae collected on different occasions over 2 years. The antigen was used for skin-testing in a dilution of 1/10,000. The tests were done on patients who showed *S. mansoni* ova in their stools; each patient was tested with one or more batches of the fresh and stored antigen, and with a saline control. Skin tests were made upon about 40 patients at each of the four periods. The results, which are tabulated, indicate that no loss of potency occurred during storage for the periods stated. Between 93 and 100 per cent. positive tests were obtained, whether fresh antigen or that stored at 6°C. for 3–12 months was used.

H. J. O'D. Burke-Gaffney.

ALVES, W. & BLAIR, D. M. **Diagnosis of Schistosomiasis. Intradermal Test using a Cercarial Antigen.** *Lancet.* 1946, Oct. 19, 556–60. [18 refs.]

Schistosomiasis is found practically everywhere in Southern Rhodesia, but the incidence varies from place to place; any plan of mass treatment must therefore be preceded by diagnosis, but the usual methods, of examination of excreta, are costly of time, staff and equipment, and may fail for several reasons: because infection may be by worms of one sex only, because there is a natural rhythm in the production of eggs, because the female worm may be in an unusual position, because the eggs may be unable to escape, because the specimens may be collected in the wrong way, or because too few specimens

may be examined. To detect *S. mansoni* in faeces, some workers break up the faeces in salt solution, and thus hatch out the eggs; the miracidia can then be observed [see SENRA, this *Bulletin*, 1942, v. 39, 698]. This is impracticable in the field in S. Rhodesia.

To overcome these difficulties, various attempts have been made to use skin tests, or other tests, in diagnosis, and the authors describe the preparation of an antigen for a skin test. Snails (*Physopsis* spp.) are collected from slow streams, and are placed in tubes of pond water, in the sun. About 10 per cent. can be seen shedding cercariae within 48 hours; these are transferred to fresh tubes (3 in. × 1 in.) containing water, one snail to each tube, and are kept thus until many cercariae can be seen—one snail may give 3,000–4,000 cercariae in 48 hours. The snail is then taken out, and the water is filtered through fine muslin, which allows the cercariae to pass; the filtrates are pooled and passed through filter paper, which holds back the cercariae. The authors aim at about 10,000 cercariae per circle of 15 cm. diameter of filter paper. These papers are dried and stored. To prepare the antigen, squares of 1 cm. are placed in a flask with enough 1 per cent. carbol saline to give about 2,000 cercariae per cc.; the flasks are shaken from time to time, and left to stand, the surplus fluid is decanted and saved, and the wet filter paper is squeezed out. This is the antigen; it is passed through a Seitz filter and diluted with an equal volume of saline, so that the final product contains 0·5 per cent. phenol and the extract of about 1,000 cercariae per cc. It is stored in the cold, and does not lose potency for 6 months. Before use, each batch is tested on a known positive and a known negative person.

The authors realize that with these snails, cercariae of *S. haematobium* are usually present, but on epidemiological grounds they think that *Physopsis* may be a host of *S. mansoni*; this is of no moment for the present work, since it is well known that there is a common antigenic factor in the schistosomes.

The test is made intradermally, the aim being to inject 0·01 cc. only. It is read in 10, 15 and 20 minutes, and a positive result is indicated by a raised, button-like weal, which may have pseudopodia. This test was carried out in 592 subjects (European and Eurafrican boys, and African young men), and stool and urine specimens were examined, several times if the test was positive. No negative skin test was encountered in a person shown to be passing eggs, and in spite of the fact that specimens from negative reactors were examined only once, the authors think that, had the test been less sensitive, some such negative results would have occurred. They therefore think it justifiable to regard negative reactors as free from infection. In spite, also, of the fact that eggs were not always found in positive reactors, the proportions showing eggs increased as more specimens were examined, and a positive test is therefore regarded as sufficient evidence to indicate a course of treatment in a patient with a suspicious history. In persons who have been treated and cured, the test may remain positive for about 2 months, but probably not much more. A persistently positive test is therefore an indication for a second course of treatment.

This test forms an admirable "screen", in mass treatment campaigns.

[See also ALVES & BLAIR below.] *Charles Wilcocks.*

ALVES, W. & BLAIR, D. M. **Schistosomiasis: a Review of Work in Southern Rhodesia in 1946.** *South African Med. J.* 1947, May 24, v. 21, No. 10, 352–7.

This is a report of the work of the Schistosomiasis Research Unit of the Public Health Department of Southern Rhodesia. In 1946 a "pilot unit", composed of Alves, with a European field assistant, 6 African snail collectors

and 8–12 African medical orderlies trained to give the slow intravenous injections of sodium antimonyl tartrate, worked in certain parts of the country. The object was to synchronize the treatment of as many infected persons as possible, with the clearance of collections of water, in the same area. In treatment, people who showed a positive reaction to intradermal injection of an antigen prepared from schistosome cercariae were given sodium antimonyl tartrate in a total dose of 1 grain to 20 lb. of body weight, the total being divided into three parts, given at intervals of 3 hours, and injected very slowly. The weights of the patients were estimated on a general appraisal. In this way, 5,455 people were treated, and there were no fatalities. One serious reaction occurred in a boy, but the drug was stopped at once, and he recovered; coughing and vomiting occurred in a number of cases, but rarely in children. One operator can handle 24 patients satisfactorily in one day, 8 each hour, but not more. In one area the cost of orderlies' wages and drugs came to 5d. per patient.

The authors quote the experience of a rapid form of treatment reported by ROSIN, of Salisbury, whose patients were Europeans. He takes them into hospital on Friday, gives a total dose of 1 grain to each 12 lb. body weight, divided into 5 or 6 doses, on the Friday and Saturday; the patients rest in bed on Sunday and return home on Monday. As much as 16 grains have been given to one patient.

One death was reported during the year: the patient was an African woman, and at post-mortem examination it was not by any means certain that the antimony treatment was the cause of death. A failure rate of 2·44 per cent. is recorded for observations lasting 3½ months; this is evidently satisfactory in a country where opportunity for reinfection is abundant.

The skin test is a very effective method of detecting infection, but it must be done and read with care. The injection must be intradermal, and the test must be read not sooner than 10 and not later than 15 minutes after the injection. This is most important. Difficulty has been experienced in the hands of some other workers, probably owing to faults of technique, and the authors say that in the individual case the test should be used as an aid to diagnosis, not as the sole criterion; but it is an admirable screen for the purpose of mass treatment.

Results with this test showed infection in 24–41 per cent. of Europeans, and in 13–89 per cent. of Africans. Children gave the lower figures in each case; the rates in adolescents and adults were similar. Adolescent girls, who do the washing and water-carrying, have high rates. This test detects infection by either *Schistosoma haematobium* or *S. mansoni*, both of which are found in S. Rhodesia.

For snail control the unit made use of copper sulphate, which in their own laboratory tests had been found to be several hundred times more effective than malachite (a mineralized copper carbonate, see MOZLEY, this *Bulletin*, 1942, v. 39, 11; 1945, v. 42, 516). A concentration of 5 parts per million of copper sulphate kills 100 per cent. of snails in 24 hours, in the laboratory. The authors use it in solution, in a knapsack sprayer. The dose is calculated for the water concerned, and the solution is sprayed with care to cover as wide an area as possible. In water in which deliberate fish culture is carried out there may be some fish mortality, and the need for fish must be balanced against the risk of schistosomiasis.

Alves [below] has pointed out that, contrary to general opinion, schistosome cercariae may live much longer than 48 hours—cercariae of *S. bovis* have been found alive for more than 120 hours, and infective at 96 hours, in the colder months, though they live only about 48 hours in the hot season.

The authors point out that the major part of control work should be done between March and October, in S. Rhodesia (the dry season); snail-gangs may be trained for malaria work in the wet season. They conclude that the experience of the pilot unit shows that "intensive attack on a given area is not only possible but practicable." [It is a vigorous attempt to deal with a massive problem.] *Charles Wilcocks.*

ALVES, W. **Recent Advances in the Study of Bilharziasis.** *Proc. Rhodesia Scient. Ass.* 1946, Apr., v. 41, 1–6.

This is a lecture in which the author describes much of the work referred to in the papers abstracted above. He records the important finding, recently made by GORMAN in the Bilharzia Research Laboratory, that schistosome cercariae will live in cold weather for 144 hours, and have been found infective at 96 hours. He points out that this fact contradicts the usual teaching that water stored for 48 hours in a tank free from snails is always safe, from the point of view of schistosomiasis. It may be so in hot weather, but not in cold.
Charles Wilcocks.

SEITZ, E. Intensive Kurzbehandlung von Schistosomiasis (Bilharzia) mit Antimonsalzen. [**Intensive Short-Course Treatment of Schistosomiasis with Antimony Salts.**] *Acta Tropica.* Basle. 1946, v. 3, No. 2, 155–7.

The author writes from Mnyusi, Tanganyika Territory. He has treated 322 patients, suffering from schistosomiasis (14 *S. mansoni*, the remainder *S. haematobium*) by an intensive course of intravenous injections of sodium antimonyl tartrate (8, or later 6, injections in 30 hours) similar to that used by ALVES and BLAIR [above, and this *Bulletin*, 1945, v. 42, 815; 1946, v. 43, 344]. The total dose was 12 mgm. per kgm. body weight; the solution was freshly made each day and each dose was diluted to 10 cc. in 5 per cent. glucose saline (later in 1·4 per cent. NaCl). The injections were given very slowly.

Of these 322 patients, 307 were examined four weeks later, and 216 eight weeks later; 4 and 3, respectively, were then positive.

No serious reactions were experienced, but some patients vomited; most of these had hookworm infestation, and low haemoglobin values. Later, therefore, the author treated those with hookworm first for that condition, before giving the treatment for schistosomiasis. [He is evidently favourably impressed.]
Charles Wilcocks.

RODRIGUEZ-MOLINA, R. & SCHWACHMAN, H. **Fuadin Therapy in 150 Cases of Schistosomiasis Mansoni with a Follow-Up Study of 70 Cases.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 117–27. [13 refs.]

The authors were stationed at an American Army Hospital in Porto Rico, where schistosomiasis mansoni is endemic. No case of schistosomiasis was detected in the large number of American troops from the U.S.A. who were there for periods up to three years. In 1944, routine examination for the Army of 15,831 local men, between the ages of 18 and 38 years, showed 2,326 (14·6 per cent.) to harbour the infection. These cases were diagnosed on a single stool examination by means of a concentration technique, and the men had probably acquired their infections in childhood. During the last two years the authors have treated 150 of these men for their schistosomiasis, with Fouadin, at the 161st General Hospital. Full examinations were made and a close watch was kept on the progress of the patients, 40 per cent. of whom were in hospital for conditions other than the schistosome infection, which was diagnosed fortuitously on routine stool examination; the remaining 60 per cent. were

suffering from mild or moderately severe manifestations of schistosomiasis. Late stages of infection with a Banti-like syndrome were not included in this study. The symptoms and signs evident in the infected are listed, and the presence of concurrent parasitic infestations is noted. A course of treatment consisted of a total of 45 cc. of Fouadin, given intramuscularly daily over a period of ten days. Toxic effects of the treatment were observed in 20 per cent. of those receiving it, but these were mild in all but two cases. In one of these latter, a severe febrile reaction, with abdominal pain and a leucocytosis (34,000 per cmm.) and high eosinophilia (79 per cent.), lasting for 10 days, followed the fourth injection (after a total of 15 cc. Fouadin). In the other, after the ninth injection, a large painful swelling occurred in a buttock, associated with a daily temperature to 103°F. and a leucocytosis (19,000 per cmm.), and eosinophilia (21 per cent.). No pus was obtained on incision, which showed only oedema and induration of the tissues ; the local and systemic conditions subsided in 6 days.

Examination of five stool specimens, immediately after a single treatment, showed that 114 (76 per cent.) of the 150 men were no longer passing ova in the stools ; 15 of 21 men re-treated with a second course of Fouadin were similarly stool-negative ; thus 86 per cent. of the men were stool-negative immediately after one or two courses of the drug. Seventy men were followed-up for one to 24 months, after treatment with from one to six courses of Fouadin (45 to 270 cc.), and 39 (55·7 per cent.) of these were found on stool examinations not to be free of their infections. The end-results of Fouadin treatment, therefore, were not particularly good ; and the undesirability of assuming the success of treatment on stool examinations done immediately after its completion was obvious. *A. R. D. Adams.*

OLIVER GONZÁLEZ, J. & HERNÁNDEZ MORALES, F. **Quantitative Determination of *Schistosoma Mansoni* Ova in Feces from Patients under Treatment with Antimonial Drugs.** *Puerto Rico J. Pub. Health & Trop. Med.* 1946, Dec., v. 22, No. 2, 210–16, 2 figs. [Spanish version 217–23.]

No quantitative determinations have yet been made which indicate the relationship between the number of live and dead eggs of *Schistosoma mansoni* passed in the faeces of untreated patients ; nor do we yet know whether dead eggs increase in number as the result of treatment or whether the treatment causes the flukes to lay dead eggs only. Existing methods of counting schistosome eggs do not give consistent quantitative results and cannot be used for counting live and dead eggs separately. In the present paper, the authors describe a counting method which does, they claim, enable reasonable quantitative determinations of live and dead eggs to be made, and these reveal interesting facts about the effects of antimonial treatment.

Briefly, the counting method is as follows : Enough of the faeces passed during 24 hours, previously mixed, is put into a displacement (Stoll) flask filled with water to the 56 ml. mark, to raise the level of the water to 60 ml. About 4 gm. of faeces produce this result. Ten glass beads are then put in, and the flask is shaken for 10 minutes. The faecal suspension is then passed through a wire sieve (50 meshes to the inch) into a large test-tube " graduated in 15 up to 45 ml. markings (Stoll tube) " and allowed to sediment for at least 30 minutes. Then the liquid above the 15 ml. mark is siphoned off and the sediment in 15 ml. of fluid is shaken. Immediately after shaking, 0·075 ml. of this sediment is drawn off with a graduated (Stoll) pipette from the middle of the tube, and placed on a slide. The total number of living and dead eggs in this sample is counted, living eggs being recognized (at a magnification of ×430) by the motion of the flame cells in them. Two samples are thus counted from each tube and

the average of the two is taken and the result can be expressed either as eggs per ml. of suspension, per gm. of faeces, per ml. of faeces or per 24-hour specimen of faeces. Conversion to a formed-stool basis is obtained by multiplication of the number of eggs by 1 if the stool examined is formed, by 2 if it is mushy and by 4 if it is liquid. SCOTT [this *Bulletin*, 1938, v. 35, 596] has pointed out that the egg output is less variable when it is expressed in terms of eggs per ml. of stool than when it is expressed in eggs per unit of time. The number of eggs per gm. of stool can be converted to eggs per ml. by the use of the common specific gravity factor 1·04, which changes stool weights to ml. [see STOLL & HAUSHEER, this *Bulletin*, 1926, v. 23, 776].

The 40 patients treated by the authors were kept in hospital for 2 to 3 weeks; they were from 18 to 33 years old and they had lived most of their lives in an area in which schistosomiasis is endemic. Eleven were treated with neostibosan, eleven with stibanose, twelve with urea-stibamine and six with anthiomaline. Three examinations of each patient were done before treatment and one each day after it until the patients were discharged.

The authors conclude that their technique makes possible a satisfactory study of the relationship between live and dead eggs in treated and untreated patients and also makes possible a grouping of people according to the degree of infection.

In 6 patients treated with anthiomaline, live and dead eggs disappeared simultaneously from the faeces and dead eggs did not persist in the faeces. Out of 12 patients treated with urea-stibamine no live or dead eggs were found in 3 patients at the end of treatment nor in the other 9 one month after treatment. These patients treated with anthiomaline and urea-stibamine remained negative for 6 and 8 months respectively. This simultaneous disappearance of live and dead eggs after treatment with these drugs suggests that the dead eggs are either laid dead by the flukes or die during their transit from the site at which they are laid. Dead eggs found in faeces are not therefore necessarily eggs which have remained for long periods of time in the intestinal mucosa. In 29 out of 40 (72·5 per cent.) patients the number of dead eggs in the faeces was greater than the number of live ones; but the relationship between live and dead eggs may be different in patients belonging to other age groups or with varying degrees of infection.

An evaluation of the efficacy of anthiomaline and urea-stibamine has been reported by HERNÁNDEZ MORALES *et al.* [this *Bulletin*, 1947, v. 44, 218]. Similar reports on the efficacy of neostibosan and stibanose will appear later.

G. Lapage.

CAIRO: MINISTRY OF PUBLIC HEALTH. MEDICAL AFFAIRS. **3rd Annual Report of the Bilharzia Snail Destruction Section, 1944–1945** [BARLOW, C. H. (Expert) & ABDEL AZIM, M. (Director). 28 pp., 4 folding maps & 2 charts. 1947, Cairo: Govt. Press.

Satisfactory progress is reported of the snail destruction campaign in the Fayoum and in Giza Province and an account is given of the results of a survey and treatment of streams in Dakhla Oasis where the infection rate in the population is about 3 per cent. The infection has been known also to exist in Kharga Oasis, half-way between Dakhla and the Nile Valley and it is proposed to begin a survey in this locality.

Conforming with the 6-year plan, discussed in the 1943 Report, the work has now been extended to the Aswan Province. Above the dam, snail surveys at Ballâna and Dakka showed heavy infestations with *Bulinus*. The topography of this area is discussed in relation to the proposed snail eradication procedure. Below the dam, snail surveys have been carried out at the important agricultural areas centering around the towns of Kom Ombo and Edfu and the whole district is now under treatment.

In the Research Section, it has been shown that during the " winter closure " a high percentage of infected snails die and that during hibernation there is a retardation of the intra-molluscan development of the parasite. The treatment of hibernating snails with copper-sulphate is slightly less effective than with actively thriving snails. The effect is less marked in *Planorbis* than in the case of *Bulinus*.

A snail survey of the Nile itself in Giza Province revealed that the Nile is only of secondary importance in restocking the irrigation streams.

J. J. C. Buckley.

CAIRO: MINISTRY OF PUBLIC HEALTH. MEDICAL AFFAIRS. **4th Annual Report of the Bilharzia Snail Destruction Section 1945–1946** [ABDEL AZIM, M. (Director) & BARLOW, C. H. (Expert)]. 28 pp., 3 maps (1 folding) & 2 charts. 1947. Cairo: Govt. Press.

The Snail Destruction Section reports improved organization and control during 1945–1946 in all the Provinces embraced by the campaign.

In the Fayoum, the use of palm-leaf traps in streams lacking vegetation, is described as advantageous and the results of this method are tabulated. The course of the campaign up to 1946 in Fayoum and Giza is illustrated graphically in regard to the ratio of streams infested to streams surveyed, and shows reductions of from 25 per cent. to 2 per cent. in Fayoum and 39 per cent. to 12 per cent. in Giza. In Aswan Province, difficulties of organization and co-ordination with agricultural and irrigation necessities have been encountered but marked reduction in the snail population has been effected. The campaign in the oases continues actively and now includes Bahariya and Kharga.

In the Research Section, the relation of age of cercariae to power of penetration has been investigated. Exposure of experimental animals to cercariae of *S. haematobium* resulted in successful infection of all the animals with cercariae of varying ages up to 24 hours. Cercariae aged 30 hours produced male worms only and no infection followed exposure to cercariae of 48 hours.

The action of various chemicals, " Methoxone " in liquid and in powder form, pure caustic potash, lime, bleaching powder and DDT was tested experimentally on snails and the weed *Potamogeton crispus* and the results are described. Taking into consideration the local cost of these agents, it is concluded that no advantage would be gained by substituting any of them for copper-sulphate.

J. J. C. Buckley.

WRIGHT, W. H., MCMULLEN, D. B., FAUST, E. C. & BAUMAN, P. M. **The Epidemiology of Schistosomiasis Japonica in the Philippine Islands and Japan. II. Surveys for Schistosomiasis Japonica on Mindanao, Philippine Islands.** *Amer. J. Hyg.* 1947, Mar., v. 45, No. 2, 164–84, 6 figs. (maps).

In the latter half of July and early August 1945 it was important to military operations to determine whether schistosomiasis caused by *S. japonicum* was endemic in the Davao area, on the east side of Mindanao. The disease had already been reported from the provinces of Surigao and Agusan, and occasional cases of infection were believed to have originated elsewhere. A survey was undertaken, examinations were made of the civilian population for hepatomegaly, hospitals were visited and their staffs were questioned in a search for suspected cases, stool examinations were made when conditions allowed, and studies of the snail population in possibly infected areas. These enquiries were made under the difficult conditions of active warfare in an area still subject to hostile Japanese interference. No evidence of the presence of the disease was found in the Davao area, and snail surveys failed to reveal the

presence of the local snail host, *Oncomelania quadrasi*. Nevertheless, later, schistosomiasis caused by *S. japonicum* was reported in American prisoners of war confined in Davao Penal Colony, situated some 12 kilometres further north than the survey party was able to penetrate. In the more central adjacent province of Bukidnon, 11 proven and 3 suspected cases were discovered in an evacuation hospital near Valencia, and another 12 proven and 1 suspected case among Filipinos in Valencia civilian hospital. No search for the snail hosts in two areas whence these cases probably derived was possible; an air survey, however, indicated a terrain suitable for *O. quadrasi*. There is reason to believe that in the coastal areas of Lanao, a province to the west of Bukidnon, there are endemic areas of schistosomiasis japonica; and survey of some riverine areas of this province also indicated foci of endemicity of the disease.

A. R. D. Adams.

FAUST, E. C. **The Effects of Cold Temperatures on the Eggs of** *Schistosoma japonicum*. *J. Parasitology*. 1947, Apr., v. 33, No. 2, 134–7.

"The known endemic regions of schistosomiasis japonica include five relatively small areas in the Japanese home islands, a vast territory in the Yangtze valley of Central China and several watersheds in South China, a small focus in Formosa, portions of the islands of Mindoro, Leyte, Samar, and Mindanao in the Philippines, and one small area in northern Celebes. In Japan and along the south coast of China the molluscan intermediate host is *Oncomelania* (*Katayama*) *nosophora*; in the Yangtze valley it is *O. hupensis*; in Formosa, *O. formosana*, and in the Philippines, *O. quadrasi*. The intermediate host in Celebes has not been identified."

The midsummer temperatures in these countries are all suitable for the hatching of *S. japonicum* eggs, but in China and Japan the winter temperatures are too low for hatching. The author decided to investigate the possibility that *S. japonicum* eggs may remain viable after long periods in the cold. For this purpose, specimens of stools of three dogs, containing *S. japonicum* eggs (the infection having been contracted in the Philippines), were investigated in New Orleans. The faeces were kept at 4°±1°C., and portions were examined at different times, to see if, after being allowed to reach 25°±4°C., they contained viable eggs, as judged by microscopic examination.

Two of the specimens had been sedimented, and were repeatedly washed in water before being placed in the cold; in the third specimen the eggs were enmeshed in mucus, and were kept in that state. At the beginning of the experiments, in the sedimented specimens, 55–57 per cent. of eggs were viable, and one specimen contained a few viable eggs after 6 months in the cold. No viable eggs were found in the mucus specimen after 27 days in the cold.

Eggs, therefore, may survive in the cold, and the author points out that he was working with strains from a tropical country where there is no frosty season; it is not impossible that in colder countries there may have developed strains even more resistant to cold.

Charles Wilcocks.

WRIGHT, W. H., BOZICEVICH, J., BRADY, F. J. & BAUMAN, P. M. **The Diagnosis of Schistosomiasis Japonica. V. The Diagnosis of Schistosomiasis Japonica by means of Intradermal and Serological Tests.** *Amer. J. Hyg.* 1947, Mar., v. 45, No. 2, 150–63. [28 refs.]

The arrival of the American Commission on Schistosomiasis in Leyte (Philippine Islands) coincided with the presence in hospital of many patients suffering from schistosomiasis caused by *S. japonicum* contracted in the island. Clinical and microscopical diagnosis of these cases was often difficult, and the development of a serological diagnostic technique was investigated. After

reviewing the literature on this subject, the authors describe how antigens for intradermal and flocculation tests were prepared from adult *Schistosoma mansoni* obtained from experimentally infected animals. The details of preparation of the various antigens are described. Attempts at diagnosis by means of the intradermal test were disappointing in early cases (4 to 5 month's duration of infection); though later, during the chronic stage of the disease and in civilians, this test proved more promising (22 positive of 28 cases.) Sera from persons of various groups including men (1) known to be infected, but untreated, (2) presumably infected, (3) not cured by chemotherapy, and (4) probably cured by chemotherapy, with a series of controls, were examined with a flocculation test. Of 104 persons microscopically diagnosed 87 (83·7 per cent.) gave a positive flocculation test; 75 of these were members of the forces and recently infected, and 58 of these gave positive readings; 29 chronic civilian cases all gave positive readings. In 11 of 70 persons suffering from a variety of conditions, but presumably free from schistosomiasis, non-specific positive readings were obtained; and three non-specific positive readings were observed in civilians from a non-endemic area of the island. A correlation between the intensity of the reaction and the severity of the symptoms was observed, all negative findings being from those either asymptomatic or showing only minor manifestations of the infection. A parallel performance of the formol-gel test in 111 military patients, 58 suffering from acute schistosomiasis and 53 from other conditions, gave consistently negative readings. In 34 chronic cases of schistosomiasis in civilians, 25 gave a positive formol-gel test; 27 civilians apparently free from the disease all gave negative formol-gel reactions. *A. R. D. Adams.*

WINKENWERDER, W. L., HUNNINEN, A. V., HARRISON, T., BILLINGS, T., CARROLL, D. G. & MAIER, J. **Studies on Schistosomiasis Japonica. 2. Analysis of 364 Cases of Acute Schistosomiasis with Report of the Results of Treatment with Fuadin in 184 Cases.** *Bull. Johns Hopkins Hosp.* 1946, Dec., v. 79, No. 6, 406–35, 3 charts.

This is a report on 364 patients (352 white U.S. troops) with schistosomiasis admitted to 118th General Hospital on Leyte Island between November, 1944 and May 1945. All except two had been infected during the reoccupation of Leyte, which started on October 20th, 1944: few cases were infected later than the end of December as circumstances changed and preventive precautions were taken.

Of 352 cases, 30 (8·5 per cent.) were classified as severe, 110 (31·2 per cent.) as moderately severe, 187 (50·3 per cent.) as mild, and 25 (10 per cent.) as asymptomatic.

The average latent period before symptoms appeared was 40 days in severe cases and 50 days in mild cases, with extremes of 26 and 58. While most of the severe and moderately severe cases showed their first symptoms in December and January, in a few, especially those with neurological disturbances, these were delayed until March, April and May. The asymptomatic cases were picked up in surveys of units exposed to infected water, or incidentally in hospital.

Ova of *Schistosoma japonicum* were found on an average about one month after symptoms appeared. In 344 (93·7 per cent. of 367) the ova were mature, in 16 (4·4 per cent.) immature, but later mature ova were found, and in 7 (1·9 per cent.) no ova were found at first, but after treatment four showed mature or immature ova; in these the diagnosis was made on history of exposure, symptoms and eosinophilia. Eosinophilia (over 500 per cmm.) was found in 322 (92 per cent. of cases); it was almost constant in moderately severe cases (96·3 per cent.), but less constant (76 per cent.) in symptomless

cases. In 3 severe cases it was not present. The degree of eosinophilia was frequently between 10,000 and 50,000 per cmm. of blood, as high as 85 per cent. of leucocytes.

Various treatment courses were given; Fouadin, from a total of 40 ml. to 80 ml. in different groups; tartar emetic; and anthiomaline. In all groups there were relapses, but only the results of treatment with a total of 40 ml. of Fouadin is discussed here. There were 210 patients in this group. The acute symptoms disappeared 2 to 3 weeks after the beginning of treatment. The ova had disappeared on the average by the 13th day. The relapse rate was approximately 40 per cent. for cases observed more than 4 weeks: in 4 cases, there was a second relapse. Most relapses were noted between the 7th and 10th weeks. The relapses were evidenced only by the reappearance of ova in the stools. In only 4 of 55 relapses was the return of symptoms noted. The ova showed no loss of viability after treatment had been given; this suggests that the action of the drug is on the adult worm.

The eosinophilia showed less tendency to fall in the relapsing cases; 60 per cent. fell compared with 83 per cent. in the non-relapsing cases. The tendency to relapse was correlated positively with the severity of the original infection.

By sigmoidoscopic examination, yellowish nodules were observed in the intestinal mucosa. Some were surrounded by a red zone, and a few showed superficial ulceration at the apex of the nodule. About half the relapsing cases showed these nodules, and they were found in 7 of 80 cases in which ova were not found in the stools. It was believed that they were evidence of relapse, and that they should be accepted as such and the patient treated. [There are many gaps in this report where data have been reported elsewhere: BILLINGS, WINKENWERDER & HUNNINEN, *Bull. Johns Hopkins Hosp.*, 1946, v. 78, 21; CARROLL, this *Bulletin*, 1946, v. 43, 1047; FRANK, *Amer. J. Psychiatry*, 1946, v. 102, 631.] *L. E. Napier.*

HOLTON, Pamela. **The Biological Estimation of Substances used in treating Cestode Infestations.** *Brit. J. Pharmacol.* 1947, June, v. 2, No. 2, 100–107, 3 figs. [15 refs.]

A method for the standardization of anti-cestode drugs is described. Mice with natural infections with *Hymenolepis diminuta* were taken; *H. nana* was also present. Extractum filicis, B.P. was given orally as an emulsion, followed 2 hours later by 1 cc. of 6·5 per cent. magnesium sulphate solution. Three hours later, the faeces were examined; the mice were killed and worms were collected from the several parts of the intestines. The worms were measured by their wet weight. Live worms from the small intestine were considered unaffected by the drug, while worms in the faeces, or large intestine, or motionless worms in the small intestine, were considered to be affected. The result was expressed as the percentage of worms affected (compared with total worms); if the probit of this is plotted against the logarithm of the dose a straight line relationship is observed. At least 15 mice should be used on each dose.

F. Hawking.

TORRANCE, H. W. **Reminiscences and Reflections on Hydatid Disease.** *J. Palestine Arab Med. Ass.* 1947, May, v. 2, No. 4 87–97. [10 refs.]

A number of useful observations on epidemiology, pathology and clinical features.

CHIFFLET, A. & LLOPART J. Equinococosis hepática y riñón derecho. [**Echinococcus Infection of the Liver in relation to the Right Kidney.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1946, Nov. & Dec., v. 29, Nos. 5/6, 509–27, 6 figs.

A general discussion.

ANDREON, E. & BERMUDEZ, O. Quiste hidatico de la región diafragmatica izquierdo. [**A Hydatid Cyst in the Left Diaphragmatic Region.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1946, Nov. & Dec., v. 29, Nos. 5/6, 487–98, 8 figs.

Report of a case.

PRIOR, I. A. M. **Hydatid Cyst of the Lung of Unusual Size. Report of a Fatal Case.** *New Zealand Med. J.* 1947, Apr., v. 46, No. 252, 109–13, 2 figs. on pls.

The cyst caused death by mechanical effect.

ARDAO, H. A. Quiste hidatico del diafragma. [**Hydatid Cysts of the Diaphragm.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1946, Nov. & Dec., v. 29, Nos. 5/6, 499–508, 5 figs.

A general discussion.

ASTRUP, A. **Uncinaria Stenocephala as a Cause of Skin Disease in Man.** *Acta Dermato-Venereologica.* 1945, Mar., v. 25, No. 5, 389–92, 2 figs.

Uncinaria stenocephala, the hookworm of certain carnivores in temperate climates, was incriminated in a case of skin eruption in a Danish labourer, aged 20. The eruption was distributed over both buttocks and extended some distance into the lumbar region and down to the upper part of the back of each thigh. It consisted of hundreds of elements varying in size from a pinhead to a pea, most of them containing a small amount of yellowish pus. A larval nematode, identified as *U. stenocephala* was found in all the samples of pus which were examined microscopically. The infection was presumed to have come from a fox-terrier which was in the habit of sleeping in the patient's bed. The adult parasites could not, however, be demonstrated in this suspected animal, so that the rather elaborate theory associating bed-wetting with skin invasion by the hookworm larvae, would seem to be somewhat supererogatory.

J. J. C. Buckley.

MUKERJI, A. K. & BHADURI, N. V. **The Treatment of Intestinal Worms with the Indigenous Drugs Butea, Embelia and Kamala.** *Indian Med. Gaz.* 1947, Feb., v. 82, No. 2, 66–9.

The indigenous Indian drugs, Butea, Embelia and Kamala are reputed to possess anthelmintic properties and have been tried in the treatment of some helminth infections, with doubtful success [this *Bulletin*, 1922, v. 19, 250; *ibid.*, 1924, v. 21, 230].

The present authors have employed the seeds of *Butea frondosa*, the dried fruits of *Embelia ribes* and *E. robusta* and the red glands and hairs of *Mallotus philippinensis*, each ground finely and administered as a paste, mixed with sugar and water.

The drugs were tested in hookworm, roundworm, and tapeworm infections. Dosage varied from 8 to 30 grains for children, 40 to 45 grains for adolescents and 60 grains or more for adults. The drugs were without effect on hookworm and tapeworm.

In *Ascaris* infections, Butea and Embelia were effective, either singly or in combination: about half of some 120 persons so treated were cured by a single dose of 60 grains or more.

It is claimed that these results indicate that Butea and Embelia are "better than santonin and equally as good as oil of chenopodium in the treatment of ascariasis".

In support of this claim, reference is made to the work of the senior author, with MAPLESTONE [this *Bulletin*, 1932, v. 29, 417], who recorded only 31 cures of 90 patients with a single dose of santonin, and 37 of 67 with oil of chenopodium.

The bulk of the drugs is a disadvantage, but may be overcome to some extent by the preparation of compressed tablets. The cost of the drugs is many times less than that of santonin and oil of chenopodium.

H. J. O'D. Burke-Gaffney.

FOSHAY, L. **The Cuticular Morphology of some Common Microfilariae.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 233–43, 2 pls. [13 refs.]

By means of the Saisawa-Sugawara silver staining technique, transverse striations were demonstrated in the cuticle of the microfilariae of the following species :—*W. bancrofti*, *W. malayi*, *L. loa*, *M. ozzardi*, *A. perstans*, *O. volvulus*, *D. immitis*, and *L. carinii*. The striations are spaced regularly at the same interval in all the species, varying only between 12 and 13 striations to each $11 \cdot 11\mu$, and they are present throughout the total length of the microfilariae.

J. J. C. Buckley.

EYLES, D. E., HUNTER, G. W. & WARREN, Virginia G. **The Periodicity of Microfilariae in Two Patients with Filariasis acquired in the South Pacific.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 203–9, 3 figs.

This paper concerns the microfilarial periodicity displayed in two ex-service patients with filariasis caused by *W. bancrofti* ; one was infected in Bora Bora in the Society islands, the other at Tonga Tabu in the Tonga group. Microfilarial counts were made by direct examination of stained or fresh blood smears made from finger punctures, except in the first series of counts on the second patient, when Knott's concentration technique was used.

On graphs and charts with which this paper is illustrated, all counts are shown as the number of microfilariae per 100 cmm., although the individual quantities examined in the first case were 25 cmm. ; in the second, the amount was as large as 1 cc.

The microfilariae, as seen in the greatest numbers during the day hours in the peripheral blood, were indistinguishable from those of the nocturnal type of *W. bancrofti*.

Peak counts (the mean for the first patient being 380, compared with 9·5 for the second) were diurnal. The results of three series of counts extending over a period of 48 hours were obtained : the first in July 1945, the second a week later, and the third in February 1946.

Examination of these graphs revealed that about 10 a.m. the number of microfilariae exceeded the mean daily count, but fell below the mean between 10 p.m. and midnight. The absolute high count occurred between 12 noon and 8 p.m., and the absolute low between 2 a.m. and 8 a.m.

These two strains of *W. bancrofti* are believed to represent infections of what is termed the non-periodic type. In view of these observations and the definite microfilarial periodicity observed, this would seem an inappropriate term, but " diurnal " would appear more descriptive. [Although this investigation represents a careful piece of work, it would seem unwise at present to change the term " non-periodic " to " diurnal."]

Compared with infections amongst Polynesians, the number of circulating microfilariae in these two American patients would appear to be small, so that definite conclusions may not be drawn. In the second case, for example, concentration methods had to be employed to demonstrate individual microfilariae, so that a possible source of error was introduced. It will be observed

that at no time were microfilariae absent from the peripheral blood, as occurs in the case of *Loa loa*. At the best it might be argued that a "relative" diurnal periodicity was observed. These observations are sufficiently suggestive to warrant their repetition in the endemic area of non-periodic filariasis. *P. Manson-Bahr.*

EYLES, D. E. & MOST, H. **Infectivity of Pacific Island *Wuchereria bancrofti* to Mosquitoes of the United States.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 211–20.

These studies were undertaken to determine the susceptibility of United States mosquitoes to a S. Pacific strain of *W. bancrofti* from a patient (an ex-service man) who became infected whilst serving on Bora Bora in the Society Islands. This is one of the very few filaria-infected American subjects in whose blood microfilariae could be found, and in this case they varied from 2 to 8 per cmm. ; in addition the period of highest microfilarial density extended from true daylight in the afternoon until after sunset, thus permitting exposure to both day- and night-biting mosquitoes.

Mosquitoes were applied during the period of greatest microfilarial density, generally between 2·0 and 4.30 p.m.

Dissections of mosquitoes were made mostly between the 10th and 20th days, since about 15 days seemed the optimum time for complete development in susceptible species.

Development to advanced or infective stages occurred in the following American mosquitoes—*Culex pipiens*, *C. quinquefasciatus* [*C. fatigans*], *C. erraticus*, *C. salinarius*, *Anopheles walkeri*, *A. punctipennis*, *Aëdes triseriatus*, *A. aegypti*, *A. atropalpus* and *Mansonia perturbans*.

In other species, *A. quadrimaculatus*, *A. maculipennis freeborni*, *Aëdes atlanticus*, and *Psorophora ferox*, infection did not progress beyond the early first larval stage.

Culex quinquefasciatus (*fatigans*) is the most consistently abundant mosquito in the southern U.S.A., but this species was less susceptible qualitatively and quantitatively than *C. pipiens* ; only 34·9 per cent. being found infected against 83·5 per cent. of the latter. In the work here reported, substantial agreement with the work of BAHR (1912) was obtained, and also with the investigations of NEWTON *et al.* [this *Bulletin*, 1946, v. 43, 52] who showed that *C. quinquefasciatus* is almost completely susceptible to the nocturnal strain of *W. bancrofti*. *P. Manson-Bahr.*

WHARTON, D. R. A. **Further Evaluation of the Skin Test for Filariasis in Man, based on Results obtained in British Guiana.** *J. Infect. Dis.* 1947, Jan.–Feb., v. 80, No. 1, 117–20.

In an earlier paper by WHARTON and STELMA [this *Bulletin*, 1946, v. 43, 1054] the conclusion was reached that a dose of 0·02 ml. of a 1 : 100,000 dilution of *Dirofilaria immitis* antigen in saline is "a suitable antigen for the diagnostic test for filariasis." These authors used also a corresponding dilution of dog serum as a control. The present paper shows that this antigen is much more highly effective and reliable when it is freshly diluted and it also confirms the necessity of using dog serum as a control.

The tests were done on 215 persons at the public hospital and the almshouse at Georgetown, British Guiana. Of these 215 persons, 193 (89·8 per cent.) were positive, 11 (5·1 per cent.) were negative and 11 (5·1 per cent.) gave indeterminate reactions. The author defines an indeterminate reaction as one which, but for use of the dog serum control, would be classed as a positive or, in a group of control subjects, as a false positive.

Of the 215 persons tested, 110 were negroes, 80 East Indians, 7 whites, 3 Chinese, 2 aborigines and 13 were "a yaried mixture". Of the 110 negroes, 90 per cent. were positive, 5·5 per cent. indeterminate and 4·5 per cent. negative. Of the 80 East Indians, the corresponding figures were 90, 5 and 5. The other groups did not contain sufficiently large samples for analysis. The reactions of the negroes and East Indians were thus practically identical. Many of the patients tested were still having filarial attacks.

Analysis of the age groups showed that widespread infection is acquired at an early age. Thus, of 23 children between 3 and 10 years old, 22 were positive. The authors of the earlier paper cited above found that only 80 per cent. of the subjects tested by them reacted to this antigen at the same dilution. The fact that at least 90 per cent. of the present series of tests were positive is ascribed by the author to the fact that every day freshly diluted antigen was used. When a group of patients was tested with a 1 : 100,000 dilution of the antigen which has been subjected to a high temperature all the previous day and possibly also through the night, many reactions were weak or negative, whereas when the same persons were re-tested with freshly diluted antigen, most of them were positive.

Throughout the series of tests, no delayed reactions occurred and the tests showed that the antigen is highly effective and safe.

Analysis of the 5·1 per cent. of negative reactions showed that 5 were negroes, 4 East Indians, 1 a white and 1 an aboriginal; these subjects represented all age-groups and none of them had ever had a filarial attack.

Many of the patients were, or had been recently, having one or other of the sulphonamides, but these drugs did not seem to affect the results. The author does not think that the antigen used for these tests can give cross-reactions with intestinal helminths and he refers to the paper by Wharton and Stelma (*loc. cit.* above) in which further evidence in support of this view is given.

Especially interesting results were obtained with 29 patients of both sexes who had had elephantiasis, usually of the legs only, but, in a few cases of the arms also, for 2½ to over 30 years. All but five of these were between 50 and 87 years old. Two of them gave indeterminate reactions because they were hypersensitive to dog serum. Of the other 27, only one was negative. This was an infirm woman 83 years old. All but two of the 26 positives gave strong reactions. The author suggests that the tissues of elephantoid patients are highly reactive and that they wall in the mature filarial worms and also block all channels by which microfilarial larvae might escape into the blood. The absence of microfilarial larvae in the blood of such patients does not, therefore, necessarily mean that all the worms in them are dead and the presence of such walled-off worms may account for the positive skin reactions which these patients may give. *G. Lapage.*

TRAVIS, B. V. **Relative Efficiency of Six Species of Mosquitoes from Guam, M.I., as Developmental Hosts for** *Dirofilaria immitis*. *J. Parasitology*. 1947, Apr., v. 33, No. 2, 142–5.

SCOTT, J. A. **Production of Quantitative Infections with the Filariae of the Cotton Rat.** *Science*. 1947, Apr. 25, 437.

The author describes a simple method of producing quantitative infections with *Litomosoides carinii*, the filaria of the cotton rat: it is claimed that this allows for more accurate experimental determinations than those previously obtained with wild-caught or mass-infected animals, and makes other studies possible, particularly in chemotherapeutic investigations.

Liponyssus bacoti, the tropical rat mites, are raised on a white rat in a metal tank surrounded by a moat containing oil. An initial 50 mites will produce a large colony in 3 to 4 weeks, and the white rat is then replaced by an infected cotton rat: the latter is removed in 10 days, and, a few days later, the mites migrate up the sides of the container.

They are taken by suction into vials and kept for at least 2 weeks after their first opportunity for an infected blood meal.

Microscopical examinations in saline are made, and mites containing larvae are kept apart and each is eviscerated under a dissecting microscope and the larvae teased out in saline. The larvae thus obtained are counted in saline in a "hookworm larva counting slide" designed by the author and listed by Arthur H. Thomas Company.

When sufficient larvae are obtained, they are drawn into a No. 15 hypodermic needle, 3½ inches long: but they should not be drawn into the attached tuberculin syringe; the syringe should contain saline to rinse the larvae out of the needle when subsequent injections are given. *H. J. O'D. Burke-Gaffney.*

SCOTT, J. A., STEMBRIDGE, V. A. & SISLEY, Nina M. **A Method for providing a Constant Supply of Tropical Rat Mites,** *Liponyssus bacoti*, **infected with the Cotton Rat Filaria,** *Litomosoides carinii*. *J. Parasitology.* 1947, Apr., v. 33, No. 2, 138–41, 1 fig.

This paper covers much of the ground of that in the preceding abstract: more technical details are given and an illustration of the tank is provided.

H. J. O'D. Burke-Gaffney.

MADSEN, H. **Biological Observations upon** *Enterobius vermicularis* (**Pinworm**). *Acta Path. et Microb. Scandinavica.* 1945, v. 22, No. 4, 392–7. [21 refs.]

The author's observations on the external migration of female *Enterobius vermicularis* indicate a biological rather than a mechanical cause for this phenomenon. It is due to the maturing of the eggs, not to loss of the attachment function of the oesophagus brought about by the encroachment of the developing uterus. He concluded, furthermore, that gravid females can emerge through the anus, lay a portion of their eggs and then retire inwards again. He discusses the nocturnal character of the migration and also the monthly periodicity of the emergences, and, with a reasoned argument, disposes of the theory that the latter is due to development of eggs which have not left the body of the host. The more probable explanation is to be found in the fact that the period of development of the worms, namely 4 to 5 weeks, corresponds more or less to the periodicity, which varies from 3 to 7 weeks.

J. J. C. Buckley.

DEFICIENCY DISEASES.

DRUMMEL, G. Le syndrome Buaki. Note préliminaire: l'action thérapeutique de la ventriculin. [**The Syndrome known as Buaki. Preliminary Note: the Therapeutic Action of Ventriculin.**] *Ann. Soc. Belge de Méd. Trop.* 1946, Dec. 31, v. 26, No. 4, 329–39.

In this paper the author records the results of treating 20 selected cases of Buaki, a syndrome characterized by hypochromotrichia and depigmentation, anaemia and oedema, and apparently similar to, or identical with, the kwashiorkor, malignant malnutrition and infantile pellagra of other writers

[this *Bulletin*, 1947, v. 44, 232]. Following the work of GILLMAN and GILLMAN [*ibid.*, 118] "Ventriculin" was the main therapeutic agent and it proved rapidly effective in the majority of cases, especially with respect to oedema and anaemia. It was combined with a full hospital diet, iron and milk, and this régime is considered the best method at present available of treating this condition.

There is no record of hepatic changes in this series. *Dean A. Smith.*

WATERLOW, J. C. **Nutritional Liver Disease in West Indian Infants.** *Proc. Roy. Soc. Med.* 1947, May, v. 40, No. 7, 347–51 (Sect. Exper. Med. & Therapeutics 9–13), 2 figs. [14 refs.]

After a preliminary examination of a small number of cases, the author describes briefly a condition which he thinks may be common among babies in the West Indies. The condition starts usually within a few months of weaning, and its main features are oedema, gross muscular wasting and fatty infiltration of the liver. Mortality has been high in the cases observed [but if the author is correct in believing that the enlargement of the liver found in 10 per cent. of an unselected group of infants represents a minor degree of this condition, then the mortality rate will be much lower]. Impairment of hepatic function was demonstrated during life by the bromsulphalein test, but not by other tests. Fatty infiltration of the liver was demonstrated by aspiration biopsy, or by examination after death.

In the small number of cases tested, no good effect was obtained by giving choline, methionine or inositol. [It is not clear whether yeast was also used without effect.] Increasing the quantity of milk in the diet to 30 oz. daily resulted in a rapid clinical improvement, with a rapid loss of oedema, a rise in serum protein, and a slow decrease in the size of the liver.

The condition as described has many resemblances to the "malignant malnutrition" of H. C. TROWELL [this *Bulletin*, 1946, v. 43, 1062] but several of the features of the latter condition are not described in the West Indian infants. *H. E. Harding.*

BARNES, G. T. **Preliminary Studies in Nutritional Deficiencies.** *J. Trop. Med. & Hyg.* 1947, June, v. 50, No. 6, 112–19.

It has long been suspected that native dietaries in Fiji may be deficient in essential nutrients. A projected nutritional survey was postponed on account of the war, but as a preliminary investigation 4,500 hospital patients were examined for evidence of nutritional disease.

Mild degrees of deficiency of B-complex factors, evidenced by angular stomatitis and burning feet, were occasionally encountered, but clinical manifestations of major degree were not found. Urine-vitamin B_1 estimations (thiochrome method) after a test-dose of 1 mgm. suggested a lowered status in respect of this factor. [Opinion is divided on the interpretation of the results of this test and even on its validity as an index of nutritional level], but no definite cases of beriberi were seen and though oedema was common, it could rarely be attributed to hypoproteinaemia.

On the other hand, anaemia, mostly hypochromic and often very severe, was extremely common and is to be the subject of a further report.

With the reservation that the anaemia may be of nutritional origin, it is concluded that the diet is not responsible for serious impairment of health or working capacity. *Dean A. Smith.*

KARK, R. M., AITON, H. F., PEASE, E. D., BEAN, W. B., HENDERSON, C. R., JOHNSON, R. E. & RICHARDSON, L. M. **Tropical Deterioration and Nutrition. Clinical and Biochemical Observations on Troops.** *Medicine.* 1947, Feb., v. 26, No. 1, 1–40, 3 figs. [46 refs.]

The belief that there is a specific deleterious effect of climate and environment upon white settlers in the tropics has been widely held for many years: the idea has been elaborated in works of fiction and travel and the syndrome of "tropical deterioration" has been described by a number of medical writers. The careful work of the present authors, broadly conceived and lucidly presented, goes far to show that there is nothing specific about "tropical deterioration". That deterioration may occur in the tropics nobody can doubt; but the authors conclude that it differs in no way from the deterioration which may occur in temperate or cold regions, and arises in response to similar conditions of stress. They did form the impression, however, that deterioration, when it does occur in the tropics, may be more disabling than elsewhere because of the natural environmental handicaps which exist in hot, humid climates.

During early 1945 the authors, working as two separate teams but using identical methods, conducted surveys on the health of troops in the tropics. The surveys included dietary investigations, medical histories and physical examinations of individuals, especially with respect to nutritional status, physical fitness tests and analysis of blood and urine samples. A Canadian unit, working in India and Burma, studied Indian soldiers and a U.S. unit, operating in several Pacific islands, studied U.S. troops, both white and coloured. The results of extensive ration-scale trials upon troops under field conditions in North America were used as standards of comparison.

Among U.S. troops, after an average length of service in the tropics of 20 months, it was found that nutrient intake and biochemical estimation results were comparable with those of troops in America, and no evidence of classical deficiency disease was found. There was moderate loss of weight averaging up to 10 lb. in troops recently exposed to prolonged combat stresses, but their fitness and morale were better than those of garrison troops.

A high degree of correlation was demonstrated between calculated intake and urinary excretion of thiamin, riboflavin and ascorbic acid.

The nutrient intake of Indian troops was difficult to assess owing to racial and religious differences. It appeared that their intakes of animal protein, riboflavin and ascorbic acid were lower than those of U.S. troops, and they were found to have lower values for haemoglobin, serum protein, serum ascorbic acid, urinary ascorbic acid and urinary riboflavin. But no cases of deficiency syndromes were seen and fitness and efficiency were good, a regiment of Gurkhas recording the highest physical fitness test scores of any troops examined.

An ocular lesion, consisting typically of hypertrophy of the conjunctival vessels with thickening of the sclera, haziness and occasionally scarring of the cornea, was found in about half the Indians examined. It showed no relationship to biochemical or other clinical findings.

The effects of prolonged exposure to combat stress were apparent in one Indian mule transport unit. The men were tired, haggard and underweight, showed many positive physical findings and had a low biochemical status and poor physical performance. There was no evidence that climate had had any specific effect in causing this deterioration, which was readily explainable by the fact that the men's rations were inadequate for the work they had to do and the stress they had to face over a continuous period of 30 months.

In a general discussion of feeding of troops in the tropics, the authors emphasize the importance of variety and palatability of food items and the

avoidance of calorie deficits, and offer no support to the proponents of supplementary vitamin administration or restricted animal protein intake.

Dean A. Smith.

DENNY-BROWN, D. **Neurological Conditions resulting from Prolonged and Severe Dietary Restriction. (Case Reports in Prisoners-of-War, and General Review.)** *Medicine.* 1947, Feb., v. 26, No. 1, 41–113, 12 figs. [288 refs.]

"The confinement of large groups of men in close captivity in war prison camps, on extremely limited diets for long periods of time, has unwittingly provided data on the effect of dietary insufficiency, on a scale that experimental medicine can hardly hope to emulate." Among the deficiency diseases observed in the camps and amongst ex-prisoners of war from the Far East were a variety of nervous disorders of which both the mechanism of causation and clinical classification are in doubt. The author, as Consultant in Neurology to India Command and Allied Land Forces South-East Asia, examined and investigated all those who suffered any neurological disability from among nearly 4,000 recently released prisoners, studied camp records and talked with camp medical officers; the present paper embodies his experiences and conclusions.

The first section of the paper is devoted to clinical descriptions of the main neurological syndromes, their onset and course.

Beriberi.—In 110 patients, the presence of symmetrical foot-drop with muscular wasting below the knee, tenderness of calf muscles, stocking area of hypesthesia and loss of ankle jerks, clearly indicated a distal type of peripheral neuritis. It was noticed that weakness in dorsiflexion, muscular tenderness and absence of ankle-jerk persist for a long time in those who are recovering and it is suggested that these three signs may be insisted upon as essential criteria for diagnosis.

Retrobulbar neuritis.—A large number of ex-prisoners gave histories suggestive of their having recovered from retrobulbar neuritis; residual disability was found in 185 cases. The constant complaint was of misting and loss of central vision, both eyes being affected. No cases of complete blindness were seen, all patients being able to count fingers in the peripheral field. Examination revealed a central scotoma, and temporal pallor of the disc in all but the mildest cases. Many showed also an area of pigmentation adjacent to the temporal margin of the disc; no other fundal abnormalities were seen.

Spinal ataxia.—Though there were a few very mild and a few very severe cases of this condition, the majority showed an unsteady, wide-based gait with staggering on turning, and Rombergism. The constant finding was loss of vibration and position sense in the lower limbs with impairment of touch and pain sensation. Muscle power and bulk appeared unaffected and reflexes were variable. These ataxic patients, 60 in number, were all afebrile and not significantly anaemic: the majority had retrobulbar neuritis but this association was not invariable.

The Spastic Syndrome.—Nine British patients were clearly distinguished from the ataxic cases by a stiff gait in which the legs tended to cross in adduction. There were extreme spasticity, exaggerated reflexes, patellar and ankle clonus and extensor plantar responses. The condition bears a close resemblance to, if not identity with, lathyrism.

In addition, *central deafness* and *laryngeal paralysis* were observed in a relatively small number of cases; there were a number of intermediate, combined or transitional conditions, and a history of "burning feet" was obtained in many.

The good diet upon release brought about rapid improvement in those suffering from beri-beri: the other neurological conditions showed little response to treatment. Some limited improvement followed injections of crude liver extract in cases of retrobulbar neuritis and spinal ataxia.

In a second section, the author gives an historical survey of nutritional disease as it affects the nervous system and a general review of the literature on the subject. It is impossible to make a useful abstract of this section: in it a vast volume of observation and record is lucidly condensed into a small compass. It is supported by a comprehensive and well-selected bibliography.

It appears, however, that all the neurological lesions encountered in prison camps have been formerly described, usually as part of the syndromes of beri-beri, pellagra (using the term in the widest sense) and lathyrism, but that they form no essential part of such syndromes and may occur independently.

[In the present series of cases, an almost constant relationship between "burning feet" and corneal degeneration was noted. This is at variance with the findings of CRUICKSHANK [this *Bulletin*, 1946, v. 43, 1159] and SMITH [*ibid.*, 1947, v. 44, 604] who described many cases of burning feet without corneal lesions, and of WOODRUFF (un-published data) who observed the converse.]

An able discussion of the mechanism and causation of these nutritional neurological lesions embraces what is known of deficiency in B-complex factors and amino-acids, and the effects of "toxic substances" (again using the word in the widest sense) such as may be operative in the causation of pellagra on a maize diet and in the causation of the syndrome known as lathyrism. The author concludes, "The disorders are highly specific in the localization of effect to different parts of the nervous system and indicate the presence of correspondingly specific, but unknown processes of abnormal metabolism. The manner in which the nervous system is damaged is reminiscent of the subacute combined degeneration of pernicious anaemia, but the accentuation was different and the anaemia absent. Detailed neuropathological studies are badly needed.

"There is as yet no indication for the use of any of the pure vitamin substances in the treatment of any of those affections. [Since this paper went to press, good results have been obtained by the use of calcium pantothenate in burning feet, GOPALAN, this *Bulletin*, 1946, v. 43, 768.] Crude extracts of yeast and liver have given good results in mild or early cases and as a source of both known and undefined factors in the vitamin B complex are the therapeutic agents of choice. . . . A balanced protein intake is as necessary as a vitamin supplement . . . the provision of fresh vegetables in the diet would appear of first importance as a prophylactic measure."

[This valuable paper should be read in its entirety by all who are interested in the neurological effects of dietary restriction.] *Dean A. Smith.*

HARIDAS, G. **Infantile Beri-Beri in Singapore during the Latter Part of the Japanese Occupation.** *Arch. Dis. in Childhood.* 1947, Mar., v. 22, No. 109, 23–33, 2 figs (1 on pl.). [18 refs.]

During the period 1942–1945, 139 cases of infantile beriberi were admitted to a civilian general hospital in Singapore. Four clinical types of the condition were recognized, the aphonic, cardiac, peripheral neuritic and pseudo-meningitic, of which the commonest combination was cardiac and neuritic. The majority of the patients were breast-fed infants of 1–4 months whose mothers showed evidence of vitamin B_1 deficiency.

Treatment by parenteral administration of vitamin B_1 in doses of not less than 10 mgm. gave satisfactory results when it could be instituted early enough.

The author draws no distinction between infantile beriberi and "breast-milk intoxication" and concludes that the two conditions, if not identical, are both caused by vitamin B_1 deficiency. [This conclusion differs from that of FEHILY [this *Bulletin*, 1945, v. 42, 139] who, on the basis of a series of clinically similar cases, suggests that the condition is caused not by primary vitamin B_1 deficiency, but by the toxic action of such intermediary metabolilte as methyl-glyoxal which are present in the milk of beriberic mothers. Decision between the two views is not at present possible. In either case, it is of the first importance, as both writers emphasize, that the disease can be eliminated by the prevention or early treatment of beriberi in pregnant or lactating women.]

Dean A. Smith.

SPRUE.

SPIES, T. D., LOPEZ, G. G., MILANES, F. & ARAMBURU, T. **Synthetic Folic Acid. The Effectiveness of a Conjugated Form in the Treatment of Tropical Sprue, Addisonian Pernicious Anemia and Nutritional Macrocytic Anemia.** *J. Amer. Med. Ass.* 1947, May 3, v. 134, No. 1, 18–20.

The following five substances have been isolated in crystalline form: (1) vitamin Bc; (2) *Lactobacillus casei* factor from liver; (3) *L. casei* factor from yeast: (4) another *L. casei* factor isolated from a fermentation residue; and (5) vitamin Bc conjugate.

Vitamin Bc and the factors from liver and yeast are identical with the synthetic product known as pteroylglutamic acid, containing one molecule of glutamic acid; but the special *L. casei* factor isolated from the fermentation residue yields three molecules of glutamic acid, and the vitamin Bc conjugate yields seven molecules. These substances can be designated pteroyldi-glutamyl-glutamic acid and pteroylhexaglutamyl-glutamic acid respectively.

The present report deals with the synthetic analogue of the former in the treatment of tropical sprue, Addisonian pernicious anaemia and nutritional macrocytic anaemia in relapse. The response to treatment is illustrated by a case history of sprue in a Cuban man aged 55 who had relapsed after treatment with liver extract and blood transfusions. From the 60th hospital day he was given, intramuscularly, 10 mgm. of synthetic pteroyldiglutamyl-glutamic acid daily for eight days. On the fifth day of treatment, the reticulocyte count began to rise, reaching a peak of 14·8 per cent. ten days after the initiation of therapy. Clinical improvement paralleled the haemopoietic response.

A similar response followed the administration of this synthetic product in two other patients, one with Addisonian pernicious anaemia, the other with nutritional macrocytic anaemia. This substance differs chemically from folic acid (*L. casei* factor) in that it has two more molecules of glutamic acid and is not excreted so promptly in the urine of subjects with macrocytic anaemia as is the *L. casei* factor.

The impression is gained that, proportionately, the response to synthetic *L. casei* factor is greater than to the conjugated form, but much of folic acid under natural conditions occurs in the latter form, and it has been shown that many patients with macrocytic anaemia are unable to convert vitamin Bc (a conjugated form) to free folic acid.

P. Manson-Bahr.

VENOMS AND ANTIVENENES.

SERGENT, Et. A propos de la vipère ammodyte. [**The Viper** *V. ammodytes.*] *Arch. Inst. Pasteur d'Algérie.* 1947, Mar., v. 25, No. 1, 71–6, 6 figs. [Refs. in footnotes.]

SARKAR, N. K. & MAITRA, S. R. **Effect of Ultra-Violet Rays on the Stability of Cobra-Venom and Cardiotoxin.** *Ann. Biochem. & Exper. Med.* 1946 v. 6, No. 2, 87–8.

Toxicity appeared to be greatly reduced by irradiation.

SARKAR, N. K., MAITRA, S. R. & ROY, P. K. **Effect of Methylene Blue on the Toxicity of Cobra Venom.** *Ann. Biochem. & Exper. Med.* 1946 v. 6, No. 2, 85–6.

Methylene blue was not found to neutralize toxicity.

HENRY-DUSTIN, Marie-Jeanne. Action antagoniste du glutathion sur les propriétés hémolytiques du venin de cobra. [**Antagonistic Action of Glutathione on the Haemolytic Properties of Cobra Venom.**] *Acta Biol. Belgica.* 1941, v. 1, No. 2, 292–3.

Glutathione in a 4 per cent. solution completely suppressed the diminished red-cell resistance in animals exposed to haemolysing doses of cobra venom.

AHUJA, M. L., BROOKS, A. G., VEERARAGHAVAN, N. & MENON, I. G. K. **A Note on the Action of Heparin on Russell's Viper Venom.** *Indian J. Med. Res.* 1946, Oct., v. 34, No. 2, 317–22.

Both *in vitro* and with *in vivo* experiments in rabbits, heparin was found to be effective in counteracting the effects of Russell's viper venom.

CILLI, V. & CORAZZI, G. Ricerche sul veleno di alcuni scorpioni eritrei (*Parabuthus liosoma abyssinicus* e *Pandinus magrettii*) e sulla preparazione di un antisiero specifico. [**Venoms of Eritrean Scorpions,** *Parabuthus liosoma abyssinicus* **and** *Pandinus magrettii.* **Preparation of Specific Antivenenes.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1946, v. 6, No. 6, 397–406. English summary.

Eritrean scorpions belong to the genera *Buthus*, *Parabuthus* and *Pandinus*. The authors' experiments have been carried out with *Parabuthus liosoma abyssinicus* and *Pandinus magrettii*, and he has studied their actions in mice, rats and guineapigs. The venoms were obtained by E. Sergent's method of grinding telsons in saline, centrifuging and adding glycerin. The m.l.d. of the former (*P.l. abyssinicus*) for mice of 25 gm. weight was 0·4–0·6 cc. (*i.e.* 4/10–6/10 of a telson); of *P. magrettii* 1·0 cc. (one whole telson). Death was preceded by staring coat, excitation and dyspnoea, followed by paralysis of the limbs. Post-mortem there was haemorrhagic oedema, gelatinous in character, at the site of inoculation, congestion of viscera and some pulmonary haemorrhages. In rats of about 180 gm., the m.l.d. was 0·5 and 1·0 cc. respectively; in guineapigs (350 gm.) 1·5–2 and 3–4 cc. respectively; the symptoms in both these animals were like those in mice, except that haemoglobinuria was a marked feature also.

The plasma-coagulating power of *P. magrettii* was much greater than that of *P. abyssinicus*; doses which would produce complete coagulation in half an hour in the case of the former would take three hours in the case of the latter. The haemolytic action of *P. magrettii* is marked, but is lacking in *P. abyssinicus*; proteolytic activity is also greater in the case of the former. Thus all three specific effects are greater in *P. magrettii* than in *P. abyssinicus*; nevertheless, the latter, by experiment, is lethal in a smaller dose.

Antivenenes were prepared by injecting donkeys with increasing doses of the venom, but this animal did not prove very satisfactory ; better results were obtained from the horse, but even with this the *in vitro* neutralizing potency did not go *pari passu* with *in vivo* protective action. *H. Harold Scott.*

GAJARDO-TOBAR, R. & VILDOSOLA, E. Anotaciones acerca del tratamiento del Latrodectismo. Los seis primeros casos curados con suero antilatrodectus. [**The First Six Cases of** *Latrodectus mactans* **Bite treated by Antivenene.**] Reprinted from *Rev. Soc. Argentina Biol.* 1944, Apr., v. 20, No. 1, 12–20.

The symptoms arising from bites by the Black Widow spider, *Latrodectus mactans*, are very severe and always serious. [A detailed account is to be found in this *Bulletin*, 1936, v. 33, 401, of a man who volunteered to be bitten on the finger in order that the symptoms and their course might be observed and studied.] Though recovery takes place without treatment, or with symptomatic treatment only, this usually takes up to a week.

Six cases are described in this paper ; the ages of the patients ranged from 13 to 40 years and the symptoms were typical in each case. Treatment with an antivenene obtained from the Carlos Malbrán Bacteriological Institute, Buenos Aires, was followed by excellent, even dramatic, results. 5·0 cc. of the antivenene was injected intramuscularly and within an hour the pain was relieved, the patient slept, recovery was complete in a few hours and the patient able to leave hospital in a couple of days or less. In one instance, 24 hours had elapsed before the antivenene was injected ; in the meantime the usual symptomatic remedies had been tried, with little if any relief.

H. Harold Scott.

DERMATOLOGY AND FUNGUS DISEASES.

GONÇALVES, A. P. Resultados da inoculação do *Treponema carateum* em boubáticos. [**Results of Inoculation of the Spirochaeta of Pinta into Yaws Patients.**] *Hospital.* Rio de Janeiro. 1947, Jan., v. 31, No. 1, 83–8 ; 91–3, 3 figs. English summary.

This is an interesting contribution indicating a certain degree of reciprocal immunity to infection by the three diseases syphilis, yaws and pinta. LEÓN Y BLANCO has recorded that *mal del pinto* develops slowly in syphilitic patients, says the author [León y Blanco has written several papers on the interrelation between pinta and syphilis ; see this *Bulletin*, 1941, v. 38, pp. 89 *et seq.*], and Dr. Gonçalves has made the experiment of inoculating yaws patients with pinta spirochaetes. Both yaws and pinta are far from common in Rio de Janeiro, but he was able to find nine cases of the former for his experiment, five in an active state with skin lesions. All were Wassermann positive. Inoculations were made intradermally with lymph from patients with pinta lesions. In two of the nine, pinta lesions were observed ; in one, 32 days after the inoculation and in the other three days later. When *mal del pinto* is inoculated into healthy persons, the incubation period before the primary lesion appears is usually 20 days. The result of the author's experiment points, therefore, to delay arising from the pre-existence of yaws in the two cases in which the inoculation succeeded, and to resistance to infection in the other seven which did not develop any pinta lesion. Not only was the primary lesion late in appearing, but the disease ran a slower course of evolution.

H. Harold Scott.

OLSON, B. J., BELL, J. A. & EMMONS, C. W. **Studies on Histoplasmosis in a Rural Community.** *Amer. J. Pub. Health.* 1947, Apr., v. 37, No. 4, 441–9, 2 maps & 1 chart. [17 refs.]

PALMER [*Bulletin of Hygiene,* 1945, v. 20, 613 ; 1946, v. 21, 665] and CHRISTIE and PETERSON [*ibid.*, 1946, v. 21, 236, 742], on the evidence of geographical distribution of persons reacting to the histoplasmin skin test, and the apparent relationship of this reaction to calcified pulmonary lesions in tuberculin-negative subjects, postulated the existence of an unrecognized, mild form of histoplasmosis. To test this hypothesis, the present authors carried out an intensive search for histoplasmosis in man and the lower animals in Loudoun County, Va., a rural area with a population of 20,000, of whom 16,000 are whites, where two cases of histoplasmosis in children (brothers) had been reported in 1945. Local physicians co-operated in the work, and persons presenting signs or symptoms consistent with histoplasmosis were sent to hospitals for mycological and radiological examinations. Search was made for infection in domestic and wild animals, especially rodents, which were trapped for examination. In this part of the work, a game warden, veterinary surgeons and private persons assisted. Two dogs on a farm, the sire and one of a litter of pups, had previously been found infected with histoplasmosis, and 603 animals belonging to 11 species, collected in the neighbourhood of the farm, were examined ; one dog, belonging to the same litter as the infected pup, and a mouse trapped in the farmhouse, were found infected. From the neighbourhood of the two human cases, 273 animals belonging to 7 species were collected, but no evidence of histoplasmosis was found in them. With ten animals from other areas, the total of 886 examined yielded only the two infections mentioned.

A total of 500 persons living in the neighbourhood of the two human cases were examined but no infection was found. Of 476 white people examined by the histoplasmin skin test and X-ray, 83 per cent. were histoplasmin-positive and 41 per cent. had calcified pulmonary lesions, but no direct association was extablished between dermal sensitivity to histoplasmin, and pulmonary calcification.

On applying a second histoplasmin test after an interval of 3 to 8 months, it was found that 7 per cent. of 58 people who were formerly histoplasmin-positive had become histoplasmin-negative, and 55 per cent. of 40 histoplasmin-negative subjects had become histoplasmin-positive.

"To date, no evidence of mild human histoplasmosis has been found in Loudoun County, Va." *J. T. Duncan.*

GAST GALVIS, A. Histoplasmosis en Colombia. [**Histoplasmosis in Colombia.**] Reprinted from *An. Soc. Biol. Bogotá.* 1947, Feb., v. 2, No. 5, 203–7, 1 pl. [Summary in English by the author.]

"A fatal case of human histoplasmosis was found in the Municipality of Cucuta, Department of North Santander. It was a woman 56 years old who died after seven days' illness, at the Charity Hospital. This is the first case which has been reported in Colombia."

SAGHER, F. **The Laboratory Aspect of Fungous Diseases of the Skin and Hair.** *Acta Med. Orientalia.* 1947, Mar., v. 6, No. 3, 68–78, 6 figs. [37 refs.]

A high percentage of those attending dermatological clinics in Palestine suffer from dermatomycoses. In order to ascertain the species of fungi implicated, cultures were made from 1,224 cases of suspected dermatomycoses examined at the Outpatient Clinic of the Rothschild-Hadassah University Hospital, Jerusalem, during 1939–46. The results of this survey are tabulated

and discussed according as the hair or skin was primarily involved, and the incidence of the fungi is compared with that recorded for other parts of the world.

Tinea capitis was the disease most frequently recorded, and in 85·2 per cent. of the cases, the causal agent was *Trichophyton violaceum*. Nearly all those so affected were Jews. The incidence of favus (caused by *Achorion* [*T.*] *schoenleini*), on the other hand, was high among Arabs and immigrants from neighbouring countries, but low among Jews. *Microsporon audouini*, which occurs so commonly in central and western Europe and in north America, was isolated only once.

Two forms of tinea cruris were recognized: a localized type caused by *Epidermophyton interdigitale* [*T. mentagrophytes*], *E. inguinale* [*E. floccosum*], or *T. purpureum*; and a generalized infection which appears to be a sub-tropical manifestation caused almost exclusively by *T. purpureum*. *G. C. Ainsworth.*

SEGRETAIN, G. Sur un *Trichophyton rubrum* d'origine africaine. [*Tricophyton rubrum* **of African Origin.**] *Ann. Inst. Pasteur.* 1947, Apr., v. 73, No. 4, 395–7, 2 figs.

Report of a case.

RAUBITSCHEK, F. **The Problems of Moniliasis.** *Acta Med. Orientalia.* 1947, Mar., v. 6, No. 3, 85–90, 2 figs. [11 refs.]

After a general discussion of moniliasis, the author reviews 460 cases of cutaneous moniliasis from the Jerusalem area, in which a study was made of the causal, or associated, yeast-like organisms. *Candida albicans* was isolated most frequently. It was obtained from 91 cases, principally of interdigital erosion and paronychia. *G. C. Ainsworth.*

BOASE, A. J. **Rhinosporidiosis.** *East African Med. J.* 1947, May, v. 24, No. 5, 199.

Report of a case in an African woman, in which the conjunctiva was involved.

MISCELLANEOUS DISEASES.

DICK, G. W. A. **Aortic Size in East African Natives.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 52–4.

"1. The circumference of the thoracic aorta of East African natives is significantly smaller than the standard measurements of aortic circumference in Europeans.

"2. The persistent thymus found at autopsy in many East African natives may be related to a hypoplastic vascular system."

MANCEAUX, A., BARDENAT, C. & SUSINI, R. Sur quelques aspects des manifestations hystériques chez l'indigène Nord-Africain en particulier en milieu militaire. [**Some Aspects of Hysterical Manifestations among North African Natives in particular in a Military Setting.**] *Algérie Méd.* 1946, July–Aug., No. 4, 321–9.

Hysteria was seen among North African natives during the recent war, as a classic histrionic disorder affecting bodily rather than mental functions. Major

fits, epileptiform and trembling attacks were seen, with somnambulism, fugues and catatonia. Static hysterical conditions, almost always of neurological order, including hemiplegias, paraplegias and other paralyses were found, sometimes superimposed upon an organic lesion, as well as local contractures, epidemic camptocormies [hysterical bending of the trunk], atony, tremor, and Parkinsonian attacks. Sensory symptoms rarely existed without motor disorders, but anaesthesia, various pains, blindness, deafness, and aphonia were encountered. The exaggerated theatrical behaviour made for ready diagnosis from organic disorders.

Isolated psychological symptoms were rarely found, but apathy, false confusion and even hallucinatory psychosis were seen superimposed upon anaesthesia.

Aetiology.—The social disruption of war, with its change in daily purpose and removal from the family setting caught the native morally and intellectually unprepared. Often nomadic, the peasant was ignorant of the motives behind the conflict and found reasons for defaulting, which an informed European or an educated native could not accept. The peasant mind is fatalistic. Prejudice, superstition, and anthropomorphic religion, credulity and suggestibility give the predeliction for somatic hysterical incidents. Barrack epidemics of hysteria, identical from one person to another, were thus possible. Laziness and apathy are typical in the climate. At his stereotyped work, the native may seem placid and unemotional on the surface, but when placed in new, dangerous, or difficult situations, he reacts violently, defensively or offensively, and having discharged emotion, will return to his former calm. If direct action is impossible because of the abstract nature of the conflict, he deals with it by hysteria. This allows him to amputate the conflict together with part of his personality, and to preserve his tranquillity.

Diagnosis.—The difference between hysteria and malingering is one of sincerity. The natives do not have the same moral judgment upon lying or duplicity as do westerners, and when they are unmasked in fraudulence, one cannot expect the same emotions. In the Service, it was necessary to suspect malingering in every atypical disorder. Malingerers would persevere in spite of argument and proof, but catching a man red-handed in the act and obtaining a confession of malingering (the usual principle before making this diagnosis), was not always possible. Catching a man out was therefore held sufficient in a court-martial or pension case, for the man to be made responsible for his attitude.

Treatment.—There were many surprises from miraculous recovery to complete failure. Persuasion alone was rarely enough and it was always necessary to fall back on physical measures. The many methods of treatment used were varied and ingenious: the less disagreeable methods did not always produce the best results, and a "heavy boot" might have greater effect than more complex treatment. The most useful treatments were: isolation, diet, with laxatives, bed, Cardiazol in sub-convulsive doses, electric shock treatment; local high tension shock gave the same results as did Faradism in the previous war.

Each treatment should be thoroughly tried, and every case is an individual affair. There is no universally applicable method for any one clinical manifestation.

Results.—The prognosis is best in paroxysmal difficulties, in special sense disorders, and in psychological upsets (somnambulism). The worst prognosis occurs in static disorders which are easily sustained by the patients. The irrecoverable forms occur, above all, in those who are particularly indifferent to external aggression. *T. F. Main.*

McDowell, F. & Varney, P. L. **Melioidosis. Report of First Case from the Western Hemisphere.** *J. Amer. Med. Ass.* 1947, May 24, v. 134, No. 4, 361–2, 1 fig.

This is an account of a case of melioidosis from St. Louis, the first to be recorded from the Western Hemisphere. The patient, a white man aged 31, had a history of an injury to his coccygeal region. The swelling which appeared was incised and shortly afterwards an acute febrile illness developed and lasted for about six weeks. The patient spent the greater part of the next eight years in hospitals and clinics, and had 78 drainage operations for abscesses about the right buttock and thigh. After four months, during which time various organisms were isolated from the sinuses, the authors made a diagnosis of melioidosis by isolation of *Pf. whitmori*. The source of infection was quite obscure. The patient had spent his life in the United States except for two years in the Panama Canal Zone 10 years before the onset of illness.

In addition to surgical measures, treatment had included local application of most of the known antiseptics, and systemic exhibition of various sulphonamides, including sulphadiazine, and large doses of penicillin. These produced no obvious benefit, and the sulphonamides were not tolerated for more than three weeks at a time. Streptomycin (16 million units in 9 days) was without effect. The patient left hospital after extensive excision of the area, followed by skin-grafting, but the authors did not feel that cure had been complete.

[It is astonishing that this rare disease should occur in one so unfortunate as to have a medical history which included all the infectious diseases of childhood, poliomyelitis, cerebrospinal meningitis, typhoid fever and trachoma.]

J. C. Cruickshank.

Wilson, H. T. H. **Tropical Eosinophilia in East Africa.** *Brit. Med. J.* 1947, June 7, 801–4. [17 refs.]

The tropical eosinophilia syndrome has been recorded on numerous occasions from India and other places [this *Bulletin*, 1945, v. 42, 589, 590 ; 1946, v. 43, 66, 252, 860 ; 1947, v. 44, 621, 753]. The author reviews the literature and distribution of this syndrome and refers to the scanty records of its existence in Africa. He then refers to seven cases in his own experience in Dar es Salaam, East Africa, six of which were encountered in a consecutive series of 34 patients suffering from chronic cough and asthma : of these, 29 were Indian, 4 Africans and one was an Arab ; all had lived on the Tanganyika coast for 2 years, and in East Africa continuously for 8 years.

The clinical, radiological and pathological findings, for the most part, followed those reported by other workers, and included some mottling of the lung fields in three cases. Leucocytosis was constant, varying from 11,000 to 34,000 cells per cmm., and the eosinophilia varied from 52 to 78 per cent. In five specimens of sputum examined by concentration methods, mites were found in three : in two of these, the mites were identified as *Tyroglyphus*.

Treatment is discussed in detail and it is shown that treatment with inorganic arsenic was dramatically successful ; the best results were obtained with a 10-day course of carbarsone followed by four weekly injections of neoarsphenamine (0·6–0·75 gm.) : this produced complete clinical cure and a rapid fall in eosinophiles during the first four or five weeks ; further treatment appeared to delay, rather than to accelerate the haematological response, so far as the eosinophile percentages were concerned. Six patients were cured, without relapses, in the three months follow-up period : the seventh regressed spontaneously.

Very detailed case-histories of all seven patients are given : the aetiology of the disease is fully and clearly discussed, and its possible relation to asthma,

Loeffler's syndrome, infectious mononucleosis, and parasitic allergy is considered; none of these features appears to provide a specific explanation. The author points out that, in most cases, there was no obvious clinical feature to distinguish these cases from bronchial asthma or recurrent bronchitis: a routine differential leucocyte count is thus essential in such cases, if tropical eosinophilia is not to be missed, though variable degrees of eosinophilia may be met with in bronchial asthma.

Most cases recorded in the literature have been found in hot and humid atmospheres: it is significant that these cases occurred in Dar es Salaam, which possesses a mean temperature of 74° to 82°F. and a relative humidity of 60 to 90 per cent.

The author rightly suggests that the condition may be relatively common on the coast of Tanganyika and probably elsewhere in tropical Africa.

[This is an admirable account of a careful study of this perplexing syndrome. The present reviewer, who had some personal contact with the author's investigations, examined the blood of two other patients in Dar es Salaam, both Indians, who showed features and results similar to those recorded by the author: attention to both was drawn by the eosinophilia encountered in the course of routine blood examinations. There is little doubt that the syndrome is commoner in the tropics than has been recognized hitherto; and in view of the gratifying response to arsenicals, much suffering might be avoided (as the author stresses) by a judicious use of differential blood-counts in puzzling cases, irrespective of the clinical features to which they may be related.]

H. J. O'D. Burke-Gaffney.

MENON, I. G. K. **Intestinal Fuso-Spirochaetosis simulating Cholera.** [Correspondence.] *Brit. Med. J.* 1947, June 28, 948.

In 1945, the writer of this letter described four cases of diarrhoea and abdominal pain, in which *Trep. vincenti* and *Fusiformis fusiformis* were found in the faeces [this *Bulletin*, 1946, v. 43, 595]. He now reports a case in which a Hindu male of 30 was admitted to hospital with a condition very suggestive of severe cholera: the only significant micro-organisms found in the faeces were *Trep. vincenti* and a few *Giardia intestinalis*.

Because of previous success with arsenicals in similar cases, the patient was given 0·3 gm. of N.A.B. He was much better next day and passed urine for the first time for 48 hours (the anuria had resisted repeated hypertonic salines). He was put on stovarsal, one tablet twice daily, and was discharged cured on the 12th day after admission.

The patient had had recurrent attacks of diarrhoea for two years before this more severe attack occurred: he had no recurrences up to eight months after the one under review.

H. J. O'D. Burke-Gaffney.

GAJARDO-TOBAR, R. & HONORATO, A. Anotaciones acerca de una epidemia de miasis humana. (Estío de 1946). [**Observations on an Epidemic of Myiasis in Human Beings.**] *Hospital de Viña del Mar.* Chile. 1947, Jan., v. 3, No. 1, 5–14, 1 fig. [24 refs.] English summary (4 lines).

An account of 81 cases: 46 occurred in the nose and 14 in the eyes: *Cochliomyia hominivorax* predominated.

GENERAL ENTOMOLOGY.

PRINGLE, G. & SINGH, H. **A Report on the Successful Control of Culicine Breeding in Sullage Waters by DDT Emulsion.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 393–402, 1 map & 1 pl.

Scum on the surface of water often prevents the spread of oil solutions of DDT. The authors experimented with DDT emulsions in scum-covered channels near Jubbulpore. After preliminary trials they diluted a " 25 per cent. DDT emulsion concentrate " [of unstated composition] with an equal quantity of clean water. This was then pumped under the water surface of the channel to be treated, by immersion of the nozzle of a knapsack sprayer. Records of successful results up to a distance of 2,200 yards from the point of application are given, but the effective distance and dose depended on the breadth and rate of flow of the channel. Ideal conditions are found in channels in which the water flows at about two miles per day, in one of which a single application of 5 litres of 25 per cent. DDT concentrate killed larvae for one and a half miles. The general principles governing dosage are discussed and the authors conclude that the method is a promising one for prevention of mosquito breeding in sullage water. [The reviewer agrees.] *G. Macdonald.*

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THEODOR, O. **On some Sandflies (*Phlebotomus*) of the *sergenti* Group in Palestine.** *Bull. Entom. Res.* 1947, May, v. 38, Pt. 1, 91–8, 4 figs. [16 refs.]

After some brief comments on the distribution of *Phlebotomus sergenti* in Palestine, Syria and Irak and its relation to oriental sore, the author then describes the male and female of a new species *P. maris-mortui*, the male of a new species *P. jacusieli* and the male of *P. palestinensis* ; some additional morphological details of the female of the last-named species are also given.

H. S. Leeson.

AGRICULTURAL RESEARCH COUNCIL. **Colonial Insecticide Research, Entebbe. Progress Report No. 2** [SYMES, C. B., Entomologist-in-Charge]. 5+91 mimeographed pp., 3 maps. 1947. London : Inter-Departmental Insecticide Committees, Agricultural Research Council, 6a Dean's Yard.

The first progress report, dated April 1946, was summarized in this *Bulletin*, 1947, v. 44, 367. The work is still in progress and it is therefore necessary to point out that owing to the incomplete nature of the investigations, the conclusions reached may not be final ; in fact some parts of the report are at the moment merely records and nothing else. Wherever in these first two reports, 5 per cent. Gammexane D929 solutions are mentioned, the gamma content should read " 0·76 per cent. to 0·77 per cent." and not as printed.

Observations on the effect of DDT on tsetse (*Glossina palpalis*) populations were made on Mbirubuziba island [location not stated] using 5 per cent. DDT in a mixture of kerosene and cotton-seed oil sprayed at 16-, 11- and 15- day intervals on vegetation at selected areas of fly concentration. A comparison of the density and patrol catches before and after the treatment showed an apparent reduction of fly of about 97 per cent. over a period of about 11 weeks. Further weekly routine searches for 8 weeks failed to produce a fly, and an exhaustive search is now in progress. Laboratory tests of treated vegetation

showed a decrease in toxicity, in some cases, from 100 per cent. to 5 per cent. in 35 days.

On Nkumba peninsula, a few miles east of Entebbe, Uganda, two applications of 5 per cent. DDT emulsion (ATSO) were followed by two of 5 per cent. DDT in diesoline at intervals of 16, 26 and 14 days. The apparent reduction of fly over 9 weeks was about 96 per cent. Since the report was written, flies have been introduced into part of this area on grazing cattle.

Two calves sprayed weekly for thirteen weeks with 10 per cent. DDT in cotton-seed oil and with 5 per cent. Gammexane in cotton-seed oil showed less gain in weight during this period than untreated calves ; there seemed also to be rapid absorption through the animals' skin, but no other signs of ill effects were observed. This matter is to be investigated further.

At Kesanje [in other parts of the Report this name is spelt " Kasanji " and " Kasenji "], Uganda, an experiment was planned to observe the effects of these insecticides on mosquitoes and malaria after treatment of the internal surfaces of African huts. Six districts were treated and one was left untreated. Descriptions are given of the areas and the various types of huts, and figures are presented showing the spleen rates, parasite rates and anopheline infectivity rates, but no attempt has yet been made to conduct an exhaustive survey. Anophelines and culicines are present to varying degrees, but the species occurring in greatest numbers are *Anopheles gambiae* and *funestus*, and *Taeniorhynchus africanus* and *fuscopennatus*. The details of the spraying procedure are described separately for each district. The surfaces of the huts treated were the walls only, the inner surfaces of the roofs only, or all the interior surfaces. The insecticides used were 5 per cent. DDT in diesoline ; 5 per cent. DDT in kerosene and cotton-seed oil ; 5 per cent. Gammexane in diesoline and 5 per cent. Gammexane dispersible powder in water.

Comparison of the weekly average numbers of total and vector species of mosquitoes, and the parasite rates before and after treatment, show a clear reduction in the numbers both of total mosquitoes and of vector species. The seasonal rise in the incidence of malaria appeared to be checked by the DDT in diesoline and by the DDT in kerosene and cotton-seed oil when applied to all surfaces, but DDT in diesoline applied to roofs only seemed to have no effect on the malaria rate. Gammexane in diesoline gave better protection than DDT and the Gammexane dispersible powder gave protection from May to August. Several aspects of this work are to be more fully investigated. Incidentally, the Africans are pleased with the effects on the mosquitoes and on bedbugs, flies and other insects ; and the people living in the control area are asking eagerly for similar facilities. Experiments of this nature are also being conducted at Jinja (Uganda) and at Kericho (Kenya).

Work still continues on the problem of the serious loss of DDT and Gammexane by absorption into treated surfaces. Preliminary notes on the progress of this side of the investigation are included in the form of a separate paper, in which are given detailed accounts of the various tests and their results. Treated vegetation, mud, thatch, plaster and lime-washed surfaces are all under examination. Considerable absorption of oil solutions and emulsions occurs on all these substances, rather more on mud walls and lime-washed surfaces than on vegetation ; there is less loss of insecticide when dispersible powders are used, and more experiments with these powders are planned.

Other matters being studied are the effectiveness of DDT on beetles (*Dermestes*) infesting hides, and the possible use of dimethyl phthalate and iso-propyl cinnamate as tsetse repellents.

A great deal of incidental information is contained in this report, and includes meteorological records, amount and cost of labour employed, types of sprayers used and field and laboratory methods. *H. S. Leeson.*

PIÉDROLA GIL, Gonzalo. Nuevos insecticidas y ahuyentadores. Su estudio, importancia y técnicas de empleo. [**New Insecticides and Repellents.**] Prólogo del Dr. Valentin MATILLA GOMEZ. Publicaciones del Instituto Español de Medicina Colonial. 247 pp., 35 figs. & 6 graphs. 1947. Madrid. Cosano, Imp.

This is an account of recent work on insecticides, for which the author has had recourse to a large body of published work.

In Chapter 1 he discusses DDT and Gammexane, their derivatives, and other recently discovered compounds ; in Chapter 2 the physio-pathology of intoxication of insects ; and in Chapter 3 the toxicity of the compounds for man, and methods of use. The techniques for evaluation of activity are described in Chapter 4. Repellents are dealt with in Chapter 5.

The value of these compounds in the prevention of infective and parasitic diseases, and in agriculture, are discussed in Chapters 6 and 7.

The book will be useful to those who desire a conspectus of work on insecticides in the Spanish language. *Charles Wilcocks.*

GORDON, I. **Improved Guns for the Delivery of Liquid D.D.T. Spray and Powder by Mechanical Compressors.** *J. Hygiene.* 1947, May, v. 45, No. 2, 173–5, 5 figs.

STEWARD, J. S. **Action of Gammexane on Arthropods of Medical and Veterinary Importance.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, May, v. 40, No. 5, 559–65. [16 refs.]

This short note summarizes experimental results with the insecticide Gammexane (*gamma* isomer of hexachlorcyclohexane). Thus :—

Diptera. Dilutions of 1 in 4 million to 8 million are lethal in a few hours to aquatic larvae (Ceratopogonidae, Simuliidae, Culicidae). Larvae of Cyclorrhapha are more resistant but the adults are very susceptible. (*Stomoxys* was controlled for three weeks by 40 mgm./sq. ft. on walls.)

Melophagus is controlled by dipping sheep in 1 : 25,000 dilution.

Anoplura and Siphonaptera are killed by dilutions of 1 : 10,000 [? applied in a dip].

Hemiptera. The lethal action is ten times as great as DDT [but persistence is not stated].

Results with Acarina :—

Argasidae. *Argas* and *Ornithodorus* were eradicated by spraying barracks with 150 mgm. per sq. ft.

Ixodidae. *Boophilus* was controlled by a 1 : 1,700 dilution.

Gamasidae. *Dermanyssus* was almost completely eradicated from hen houses by a single spraying with 1 in 2,500.

Astigmata (Sarcoptoidea). A single immersion for half a minute in 0·01 per cent. is effective against *Notoedres muris.*

Single spray treatment of chorioptic leg mange in horses and neck and rump mange in cattle destroyed most of the acari and gave much clinical improvement with dilutions up to 1 in 40,000. *J. R. Busvine.*

LABORATORY PROCEDURES.

WATSON, J. M. **A Modification of the Zinc Sulphate Centrifugal Flotation Technique for the Concentration of Helminth Ova and Protozoan Cysts in Faeces.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 43–5.

The author describes two modifications of the Faust flotation technique.

In the first place, sieving of the faecal sample is omitted: not only is the advantage of sieving negligible compared with the labour and time involved, but there is evidence that any form of straining may reduce the number of ova detected.

Secondly, the disadvantages of requiring special fittings to hold the receiving cover-slip after final centrifugation have been overcome by keeping the cover-slip in contact with the top of the centrifuge-tube by means of a film of Mayer's egg albumin. This albumin (white of egg 50 cc.; glycerine 50 cc.; salicylate of soda 1 gm., shaken and filtered) is smeared lightly on the underside of the cover-slip, which is thus attached firmly to the rough-ground surface of the tube, because of the sticky film, combined with the centrifugal force developed. An ordinary No. 1 cover-slip suffices, but care must be taken to see that it is centrally placed over the centrifuge-tube before spinning is begun.

This modification has the further advantages that cysts and ova tend to stick to the albuminous layer on the cover-slip, and that this film forms a seal between the cover-slip and the tube, thus preventing the leakage of fluid and access of air.

The complete modified method as used by the author is briefly the following:—

1. The small faecal sample, about the size of a pea, is broken up into a fine suspension in distilled water in the centrifuge-tube.

2. The suspension is centrifuged for 3 minutes at 1,500 r.p.m. (for an ordinary centrifuge with a 5½ inch radius). The supernatant is removed and the process repeated, usually twice, until the fluid is clear.

3. Zinc sulphate solution (33 per cent. $ZnSO_4$–$7H_2O$, specific gravity 1·18) is poured into the tube and the sediment re-suspended: more solution is added until the meniscus is level with the top of the tube.

4. A chemically-clean circular cover-slip, of slightly greater diameter than the tube, is lightly smeared with Mayer's egg albumin and this surface is pressed symmetrically on top of the centrifuge-tube: the development of air-bubbles should be avoided.

5. The suspension is centrifuged for 3 minutes at 1,500 r.p.m.; the cover-slip is rapidly removed and placed, face downwards, on a drop of Weigert's iodine on a slide.

[The many advantages described in this modification indicate that it might well be adopted as a standard routine method.] *H. J. O'D. Burke-Gaffney.*

HOOD, Marion. **The Practical Handling of Parasitology by the Clinical Pathologist.** *Southern Med. J.* 1947, June, v. 40, No. 6, 523–8.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

SOUTH AFRICA, UNION OF: **Annual Report of the Department of Public Health for Year ended 30th June, 1946** [GALE, G. W., Secretary for Health]. 55 pp., 1 folding chart & 1 folding map. 1947. Pretoria: Govt. Printer.

Though this report is presented by Dr. Gale, during the period which it covers Dr. Peter ALLAN was still Secretary for Public Health, as he did not

retire until 1st July, 1946. The report starts with an appreciation of all that Dr. Allan had done in building up the Department and especially his activities regarding tuberculosis in his earlier years of office.

Vital statistics need not be entered into in detail here. The European population has increased by 35,000 and there has been improvement all round; the birth rate has risen from 25·94 to 26·23 per mille and the death rate has fallen from 9·53 to 9·33; the infant mortality rate has fallen from 45·60 per thousand live births to 42·53, the lowest on record and less than half that of a quarter of a century ago (90·07) when returns were first kept; and the maternal mortality has dropped to 2·20 per thousand live births registered, 0·65 below that of the previous year and again the lowest on record.

Notifications of epidemic diseases show a most satisfactory decline. A few figures may be given (the bracketed figures being those of the previous year): *Smallpox* 1,721 (3,317); *typhus* 778 (2,909); *plague* 4 (39), the lowest for more than 20 years; *diphtheria* 2,738 (3,046) with 184 (245) deaths; *infantile paralysis* 216 (1,380). *Enteric fever* mars the picture with a total of 6,032 (3,470), an increase of 73 per cent. *Tuberculosis*, ascribed largely to under-nourishment and overcrowding, is still a major problem and is thought accountable for some 20,000 deaths annually. Development of new industries led to influx of natives, but as no additional accommodation was provided, overcrowding of existing dwellings was the natural sequel. The returns are presented in much detail; cases and deaths are shown for each decade, in a table in which subdivisions are made according to race.

The general health improvement is due in large part to the new Health Centre Service. This, however, has not yet come to its full development and the older system of district surgeoncies is still maintained. There are six pathological laboratories, namely at Johannesburg, Cape Town, Durban, Port Elizabeth, East London, and Bloemfontein, which dealt with between 600,000 and 700,000 specimens during the year. At the Vaccine Institute, Rosebank, antivariola lymph is prepared; 310 calves were successfully vaccinated and close on 218 litres of lymph obtained. During the year, penicillin and biological products derived from human blood were brought under control of the Therapeutic Substances Regulations.

A few diseases call for special remarks: *Amoebiasis*, made notifiable at the beginning of 1945, accounted for the greatest number of notifications of infective disease in Natal and Zululand, *viz.* 199 per 100,000; in Durban alone, 4,410 cases were notified, nearly two-thirds of the total, 6,637. *Diphtheria* came next, with 29·6 per 100,000. *Schistosomiasis*, widespread in the Union, is all too common among schoolchildren in the Pretoria district. At Klipdrift school some 17 per cent. were infested; at Alma, as many as 22 per cent. The death rate from *cancer* continues to rise and this year has reached the peak figure of 111·96 per 100,000. It is hoped that the Health Centres, by introducing periodic examinations, will bring about earlier diagnosis at a time when treatment may be availing. *Diphtheria*, as already stated, is still rife, an average of 7 cases being notified daily, but immunization is proceeding apace and it is gratifying to note that one-third of the mothers have their children immunized on their own initiative. APT is mostly used, a first dose of 0·2 cc. being followed in 4–6 weeks by 0·5 cc. Of 2,214 *leprosy* patients in the five Union hospitals, only 65 (2·9 per cent.) are Europeans. Epidemic *malaria* in Natal and Zululand is associated with *A. gambiae*. There is organized control over the coastal areas to the south, but infection is spreading westward where such control is not in force. Measures adopted in the different districts are detailed, and quinine depots have been established. A map reproduced in the report shows clearly the distribution of cases of *plague* during the last quarter of a century. The most active foci at present are in the northern Orange Free State, the

border of the Transkei and the districts of Uitenhage and Port Elizabeth; none was reported from Basutoland or S.W. Africa. A Plague Research Laboratory has been established and there is also a mobile laboratory for facilitating field work. *Enteric fever* constitutes a serious problem; it has been referred to incidentally above. Flies and carriers are important as vector and source. An outbreak in Brakpan in November and December 1945 involved some 300 persons, mostly Europeans; it was found to be due to milk infected by an African working at one of the dairy farms supplying the depot. The question of pasteurization of milk was debated, but there is no little opposition and even more indifference to its introduction. *Venereal disease*, as would be expected, varies much from district to district; the incidence of gonorrhoea is low, but that of syphilis tends to rise and patients cease attendance when their symptoms improve and before cure is complete, and the warning is again issued of the "danger that both the public and medical profession may be lulled into complacency" by the new and improved methods of treatment.

The Department is fully aware of the chances of introduction of *yellow fever* into the Union, and takes all precautions. There is a yellow fever laboratory at Rietfontein, run in association with the South African Institute for Medical Research, making vaccine and carrying out immunity tests.

The subjects of Nutrition and Housing Schemes are treated in some detail, particularly the latter, and remarks are made on rural sanitary conditions in Cape Province, Natal, the Orange Free State and the Transvaal, and also on maternity, child welfare and the dental service.

A few words must be added on the setting up of Health Centres as a basis of a National Health Service, recommended by the Gluckman National Health Commission. The Polela Health Unit was established in 1940 and a training scheme started, to educate a "health personnel". Decision was reached after much discussion that Durban would be the most suitable place for headquarters of the Institution, because Durban and its environs included all races, varieties of housing schemes and industrial conditions and therefore offered opportunities for varied training and the practice of social, therapeutic and preventive measures. The year under review was spent mainly in laying the foundations of the Service and drawing up a programme. Several centres were inaugurated and others are projected. Observations are made on some of the more important, Polela, Newlands and Springfield near Durban; Bushbuckridge in the Transvaal low veldt; Grassy Park, Knysna, Umtata and Alexandra; special matters were taken up in each of these. [See also GALE, this *Bulletin*, 1946, v. 43, 1083.] Finally, the *Nursing Service*: At the end of the year there were 10,697 nurses on the register of the South African Nursing Council, and 7,232 midwives. The standard of nursing examinations is indicated by figures which show that about one-third of the candidates failed at some stage.

The report contains several other points of local rather than of general interest. The whole, however, goes to show that the Union Department of Public Health under the new Secretary, Dr. Gale, is fully maintaining the high standard of activities set up by Dr. Peter Allan. *H. Harold Scott.*

SICÉ, A. L'oeuvre médico-sociale de la France dans ses territoires d'outre-mer. [**Medical and Social Work in French Overseas Territories.**] *Bull. Acad. Nat. Méd.* 1947, v. 131, Nos. 15/16, 271–6.

A sketch, with much information in a condensed form, of the conditions, mainly medical, partly social, existing in the French colonies. As in the colonies of other countries, the question of nutrition is important and many diseases are aggravated by mal- or innutrition. A fact not generally known is stated, that tribes living chiefly on millet are harder workers and more resistant to

disease than are those living on manioc (cassava). In Indo-China the great development of rice-growing in recent years is converting the country into one " vast rice-field " and so putting an end to the seasonal returns of famine. Attention is being paid to infant welfare, but scarcity of midwives, nurses and health visitors sets a limit to what can be done, Short courses are given to instil certain women with the main principles, but on return to their villages these soon grow hazy in their knowledge and revert to the old customs. Nevertheless, improvement has taken place. In Equatorial Africa, consultations for infants have risen from 6,000 in 1935 to 100,000 in 1945, and for those from two to five years of age from 14,000 to 120,000. Orphanages have been established for rescuing and educating abandoned half-castes, and helping them to earn their own living. Doctors, midwives, male and female nurses are being trained at schools established at Hanoi, Antananarivo and Dakar.

As regards diseases: *Smallpox* has been largely conquered. In August 1943 some cases appeared at Fort Lamy, imported by nomads. Vaccination was intensified, but was disappointing, at least at the beginning. Vaccine obtained from Paris which had been kept in reserve gave only 33 per cent. positives; it had been kept too long. A dried vaccine from America proved useless. Finally, the authorities at Lake Chad set the Fort Lamy centre going again and a satisfactory lymph was produced. During 1945, 626,873 smallpox vaccinations and 78,291 combined smallpox and yellow fever vaccinations were performed.

Human trypanosomiasis is decreasing in most districts. In French West Africa, 4½ million persons were seen [period not stated] and 300,000 were diagnosed and treated. Fresh infections, which in 1938 numbered 2·57 per cent., were in 1945 only 0·4 per cent. In French Equatorial Africa, of a total population of about 3,800,000, nearly 40 per cent. (1,472,700) were examined [period not stated] and 7,600 cases diagnosed. Fresh infections have fallen from 0·7 per cent. in 1941 to 0·43 per cent. in 1945.

Malaria remains a serious menace. In Madagascar and Réunion the scourge is far from being mastered. In 1945, 26·1 per cent. of all hospital patients seen were suffering from malaria [type not stated]. The small-scale measures hitherto undertaken are quite inadequate.

Leprosy is still rife, owing partly to general malnutrition and partly to promiscuous contact. Certain centres exist, as at Bamako in French West Africa, and Mozoariva in Madagascar, where agricultural colonies are established and seem to be a success.

Plague is under control both in West Africa and Madagascar and a live vaccine, E.V. strain, prepared at the Pasteur Institute, Antananarivo, is used. More than three million have been vaccinated with it and the number of cases of infection has fallen from 681 in 1939 to 184 in 1945.

Yellow fever occurs only as isolated cases in the villages and no connexion can usually be traced between them. In French West Africa, there were 23 cases in 1941, but only two in 1944, neither having been vaccinated. The total of vaccinations (Laigret's vaccine isolated by him with Sellards) has increased from eight millions in 1941 to fifteen millions in 1945. In French Equatorial Africa, there has been no case since the nine recorded in 1941.

Cholera is clearly retrogressing and the *dysenteries* and *tuberculosis* cause no alarm [no figures given]. *Syphilis* is still rife and plays no small part in infant mortality.

Among new sera prepared is one against the venom of *Naja melanoleuca* which is highly toxic, but has feeble anticoagulant and haemolytic actions; that of *Dendraspis jamesoni* is slightly less toxic and has weak haemolytic and proteolytic actions but is markedly anticoagulant.

Lastly, a permanent Commission has been appointed for the study of ethnological problems. [This is an interesting summary of conditions in the French tropics.] *H. Harold Scott.*

BASU, N. K.; LAL, S. B.; SHARMA, S. N. **Investigations on Indian Medicinal Plants. Part I.** *Asteracantha longifolia* [BASU & LAL]. *Quart. J. Pharm. & Pharmacol.* 1947, Jan.–Mar., v. 20, No. 1, 38–9. *Trianthema monogyna* **Linn** [BASU & SHARMA]. *Ibid.* 39–41. *Boerhaavia diffusa* **Linn** [BASU & SHARMA]. *Ibid.* 41–2.

BOOK REVIEWS.

BUXTON, Patrick A. [C.M.G., F.R.S., Director, Department of Medical Entomology, London School of Hygiene and Tropical Medicine, Professor of Medical Entomology, University of London]. **The Louse. An Account of the Lice which infest Man, their Medical Importance and Control.** 2nd Edition. pp. viii+164, 47 figs. 1947. London: Edward Arnold & Co. [10*s.* 6*d.*] [This review appears also in *Bulletin of Hygiene.*]

It is nearly eight years since the first edition of this work was published. The new edition records the extensive advances in knowledge of the louse achieved during the war years. The revision was completed early in 1945 and includes published work up to the end of 1944. It is nearly half as long again as the first edition, but this increase is compensated by the deterioration of paper and binding so that the size and the weight of the book remain unchanged.

Comparing the two editions one is impressed by the little we knew about the louse and how to control it in 1939. Every aspect of the subject, morphology, physiology, ecology and control, has been studied in these last years. There is new knowledge of the mouth parts of lice, and their sense organs. Their sensory physiology and behaviour under controlled conditions have been described in detail. There is room for increased knowledge of their behaviour in their normal environment, but here also advances have been made. We have detailed information on the distribution of lice in the various seams and regions of the clothing and a little is known of their movements in this environment. The temperature relations of the egg, that is, the temperatures at which development and hatching can occur, as well as the lethal high temperatures, are much more fully known. It appears that there is no combination of temperatures under which eggs can hatch as late as one month after laying. The evidence collected during the war supports the view adopted in the first edition that the head louse and body louse are well defined biological races or "species in the making" and that the conversion of one sort into the other does not readily occur. The vexed question as to whether some persons are more susceptible to infestation than others is still not fully resolved. Some progress has been made in feeding lice through membranes, but this technique does not seem to have been put on a really practical basis. Several generations have been reared on the rabbit when the skin was closely shaved.

It is in the chapter on the control of lice that the most spectacular transformation has taken place. The homely methods of control which figured in

the first edition are now of little more than historic interest. The hopes which the author expressed in 1939 that we might find an insecticide " capable of being applied to a clothed unbathed soldier " and " substances with which garments might be impregnated " have now been realized. In this chapter, which has been entirely re-written, will be found details of the uses and methods of application of DDT as well as all the other insecticides that have been used with more or less success during the war: the thiocyanates, notably the " medicated (lethane) hair oil " of the National War Formulary, developed by the author for the control of head lice; diphenylamine; bis-ethyl xanthogen; the improved pyrethrum powders; gammexane, etc.; as well as the modern methods of fumigating clothing and bedding. The first edition was a good book; great advances in knowledge have made the second a far better one.

V. B. Wigglesworth.

WAR OFFICE. **Memoranda on Medical Diseases in Tropical and Sub-Tropical Areas.** Eighth Edition. 396 pp., 76 figs. & 37 pls. 1946. London: H.M. Stationery Office. [7*s*. 6*d*.]

The eighth edition of this manual is a great improvement on any former edition, for a number of reasons. It is now bound in stiff covers of admirable quality, and is printed throughout on art paper such as is rarely seen at the present time. The pages are somewhat bigger than in the previous editions, and the print is much better. Many new illustrations by Mr. J. H. GRUNDY have been incorporated, both line and half-tone drawings, and lovers of clear draughtsmanship will take delight in the expressive accuracy of his entomological drawings. They have been made from actual specimens, and they contain nothing inessential, and no guesswork.

The layout of the book is as before, with some modifications; diseases are still dealt with in alphabetical order, and paratyphoid fever, therefore, is separated from typhoid fever by a hundred pages of plague, rickettsial infections, sulphonamide drugs, tropical eosinophilia and other items beginning with appropriate letters. But kala azar and oriental sore are at last brought together under the heading of leishmaniasis, and amoebiasis now includes liver abscess. But the alphabetical system (*pace* the remarks in the preface) has nothing to commend it. In this preface, Sir Alexander HOOD writes that the book " does not claim to be more than a series of miscellaneous memoranda arranged in alphabetical order ", but 6 new sections have been added (infective hepatitis, leprosy, nutritional diseases, sulphonamide drugs, tropical eosinophilia, and the uses of DDT) and it is now almost a text-book (though this is specifically disclaimed), with a reasonable index. The place for a chapter on arthropod pests should not, the reviewer feels, be between chapters on ancylostomiasis and beriberi, nor that on the sulphonamide drugs between sprue and tropical eosinophilia. A more reasonable order of contents could very easily be made.

Much of the book has been rewritten, and the results of war experience have been incorporated, especially in relation to malaria and typhus, the dysenteries and sprue; but the chapter on filariasis is inadequate, in view of the apprehensive interest it created at one time in the troops, and of the fact that the fears were unjustified. In the description of schistosomiasis the Nile is referred to frequently, but the prevalence of the disease throughout the rest of Africa, though mentioned, is not stressed; yet this disease caused trouble enough during the war. On the other hand, treatment is reasonably well covered. The book is, of course, chiefly concerned with the clinical features of the diseases described, and though prevention and prophylaxis are referred to, and in some parts emphasized, they are subsidiary.

Charles Wilcocks.

EDGE, P. Granville [O.B.E., D.Sc., etc.]. **Vital Statistics and Public Health Work in the Tropics including Supplement on the Genealogy of Vital Statistics.** Foreword by Major GREENWOOD, D.Sc., F.R.C.P., F.R.S., etc. 2nd Edition. pp. xii+268. 1947. London: Baillière, Tindall & Cox, 7 & 8 Henrietta Street, W.C.2. [15s.]

That there is an urgent need for reliable—indeed, sometimes, for any—vital statistics from tropical countries would hardly be denied. The development of appropriate public health measures and the application of preventive medicine are to a considerable extent dependent upon them. It will more often, however, be argued that it is quite impossible to gather them amongst native races and that in urging their importance the statistician merely lives in a world of dreams. It is more often true that the statistician is no less conscious of the difficulties than his non-statistical colleague, and he is also aware of two other things—that if nothing is attempted before perfection is attainable then nothing will *ever* be done, and that dependable results can often be reached by sampling methods when a full account is impossible. That something *is* being done, that more persons today are alive to what can be a fascinating as well as a utilitarian subject of study, is indicated by the demand for this second printing of Dr. Granville Edge's admirable handbook. In it he discusses very clearly how one may set about answering arithmetically the, superficially, simple questions he himself propounds—"*what* is happening, *how* and *when* do specific happenings occur, *why* do these specific happenings occur?" That the approach is realistic and avoids a mere sponsoring of western procedures is ensured by Dr. Edge's personal experience of tropical conditions and his wide knowledge of the medical and vital statistical reports issued from British Colonial Possessions. To the present edition he has added a supplement entitled the Genealogy of Vital Statistics in which, in some 75 pages, he traces the rise (and at times the fall) of vital statistical thought and activities. To workers in the tropics, this addition will certainly be of interest, for it briefly reveals how systems of recording naturally grew from small beginnings, and indicates how some of the pioneers could put to valuable use the very imperfect material at their disposal. *A. Bradford Hill.*

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